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(54) piperidines as anticholinergic agents

Piperidin Derivate als anticholinerge Linkstoffe

Dérivés de pipéridine comme agents anticholinérgiques

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(73) Proprietor: **Eisai Co., Ltd.**
Tokyo (JP)

(72) Inventors:
- **Sugimoto, Hachiro**
  Kita-ku, Tokyo (JP)
- **Tsuchiya, Yutaka**
  St. Fort Lee, New Jersey, 07024 (US)
- **Higurashi, Kunizou**
  Tokyo (JP)
- **Karibe, Norio**
  Tokyo (JP)
- **Iimura, Youichi**
  Tsukuba-shi, Ibaraki (JP)
- **Sasaki, Atsushi**
  Tsukuba-shi, Ibaraki (JP)
- **Yamanishi, Yoshiharu**
  Ryugasaki-shi, Ibaraki (JP)
- **Ogura, Hiroo**
  Tsuchiura-shi, Ibaraki (JP)
- **Araki, Shin**
  Moriyamachi,Kitasouma-gun (JP)
- **Kosasa, Takashi**
  Yawaramura, Tsukuba-gun (JP)
- **Kusota, Atsuhiko**
  Tsuchiura-shi (JP)
- **Kozasa, Michiko**
  Yawaramura, Tsukuba-gun (JP)
- **Yamatsu, Kiyomi**
  Kamakura-shi, Kanagawa (JP)

(74) Representative:
Hansen, Bernd, Dr. Dipl.-Chem. et al
Hoffmann Eitle,
Patent- und Rechtsanwälte,
Arabellastrasse 4
81925 München (DE)

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Remarks:
Divisional application 96110252.2 filed on 25/06/96.

EP 0 673 927 B1

Description

[0001] The invention relates to a cyclic amine compound and a therapeutical composition for use in the medical treatment of senile dementia.

(Statement of Prior Arts)

[0002] With a rapid increase in the population of aged people, the establishment of the therapy for senile dementia, such as Alzheimer senile dementia, is eagerly desired.

[0003] Various attempts have been made to treat the senile dementia with a drug. So far, however, there has been no drug which is very useful for the treatment of these diseases.

[0004] Studies on the development of therapeutic agents for these diseases have been made from various aspects. Particularly, since Alzheimer senile dementia is accompanied by the lowering in cholinergic hypofunction, the development of the therapeutic agent from the aspect of an acetylcholine precursor and an acetylcholinesterase inhibitor was proposed and is in fact attempted. Representative examples of the anticholinesterase inhibitor include physostigmine and tetrahydroaminoacridine. However, these drugs have drawbacks such as an unsatisfactory effect and the occurrence of unfavorable side effects. At the present time, there are no decisive therapeutic agents. EP-A-0 229 391, prior art in accordance with Article 54(3) EPC, discloses piperidine derivatives of the formula R^1-X-A-R^2 and their use in the treatment, prevention, remission and improvement of various types of senile dementia, especially Alzheimer's disease. R^1 may be a substituted or unsubstituted benzene; the bridging group X may be -$(CH_2)_n$-, -NH$(CH_2)_n$- or -NH-CO-$(CH_2)_n$- wherein n is an integer of 1-7; A may denote a ring such as para-substituted pyridine; and R^2 may represent a substituted or unsubstituted benzyl group.

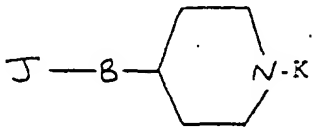
[0005] JP-A-7 785 174, J. Pharm. Pharmacol., 1969, 21(7), 434-40, GB-A-1323508, FR-A-1517670 and DE-A-2 148 959 disclose piperidine derivatives.

[0006] In view of the above situation, the present inventors have made extensive and intensive studies on various compounds for many years with a view to developing a drug which has a persistent activity and a high safety.

[0007] As a result, the present inventors have found that a piperidine derivative represented by the following general formula (XXV)' can attain the desired object.

[0008] Accordingly, the present invention is concerned with the use of a cyclic amine compound as defined in Claim 2, 3, 4 or having the following formula (XXV)'

or a pharmacologically acceptable salt thereof:

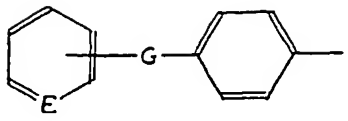


(XXV)'

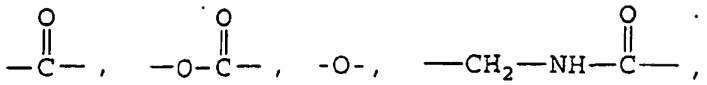
wherein:
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

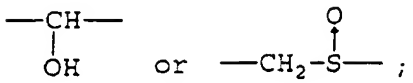
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



and E is a carbon or nitrogen atom;

the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$,$-(CH_2)_2-CO-NH-(CH_2)_r-$, -CH(OH)-$(CH_2)_r-$, r being zero or an integer of 1 to 6, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group,

or a pharmacologically acceptable salt thereof,

for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity.

[0009] Specifically, the compound of the present invention represented by the following general formula (XXV) has great advantages of having strong and highly selective antiacetylcholinesterase activity, increasing the amount of acetylcholine present in the brain, exhibiting an excellent effect on a model with respect to disturbance of memory, and having a persistent activity and a high safety when compared with physostigmine which is a conventional popular drug in the art, which renders the compound of the present invention very valuable.

[0010] The compound of the present invention was found based on the acetylcholinesterase inhibitory action and, therefore, is effective for treatment and prevention of various diseases which are thought to be derived from the deficiency of acetylcholine as a neurotransmitter in vivo.

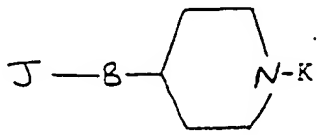
[0011] Examples of such diseases include various kinds of dementia including Alzheimer senile dementia and further include Huntington's chorea, Pick's disease, and ataxia.

[0012] Therefore, the objects of the present invention are to provide a novel piperidine derivative effective as a pharmaceutical, particularly for treatment and prevention of central nervous system diseases, to provide a process for preparing the same, and to provide a pharmaceutical comprising the same as an effective ingredient.

(Summary of the Invention)

[0013] According to a first aspect, the present invention provides a cyclic amine compound having the following

formula (XXV) or a pharmacologically acceptable salt thereof:



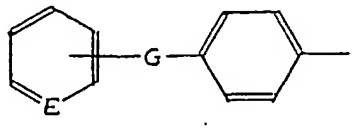
(XXV)

wherein:

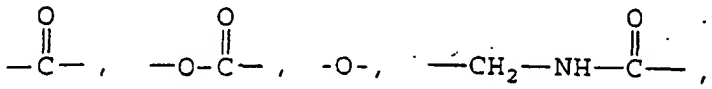
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

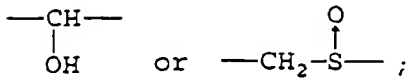
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,

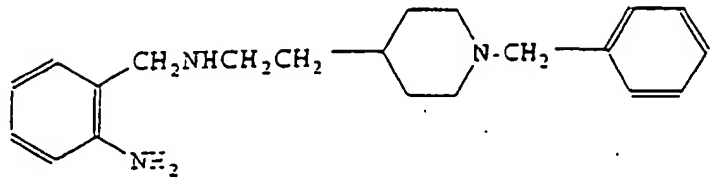


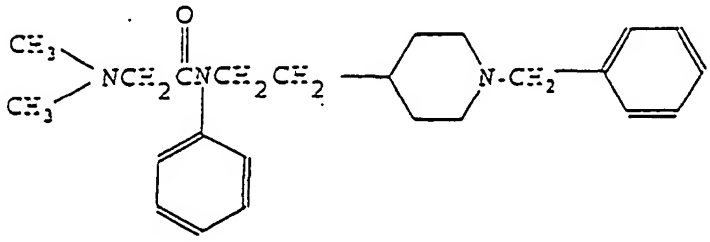
and E is a carbon or nitrogen atom;

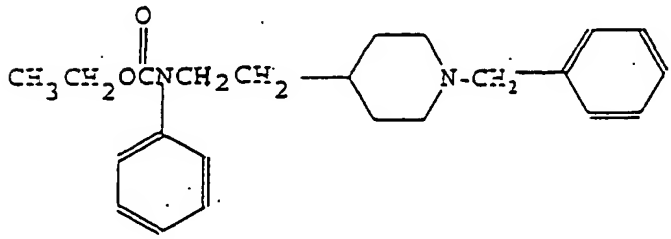
the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6 with the proviso that if B is $-NR^4-(CH_2)_r-$ then r is not zero, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

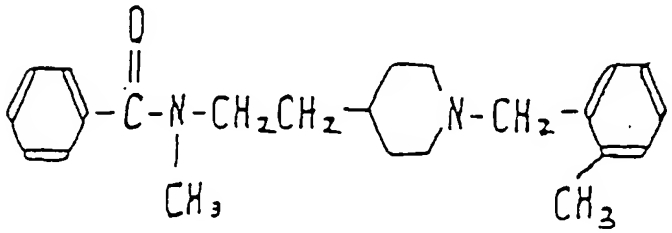
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

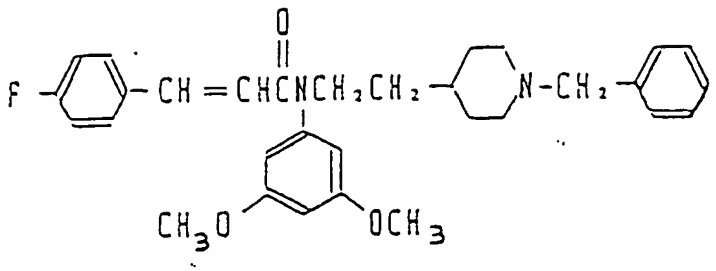
[0014] According to a second aspect, the present invention provides a cyclic amine compound of any one of the formulae:

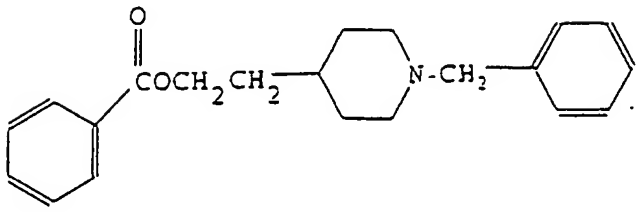


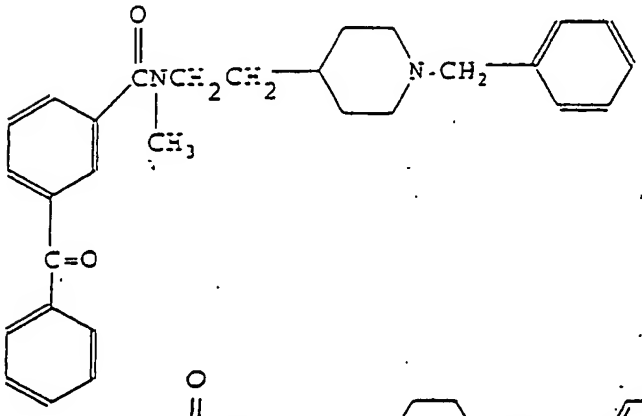


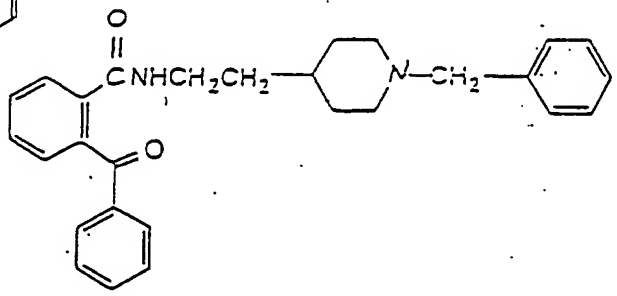


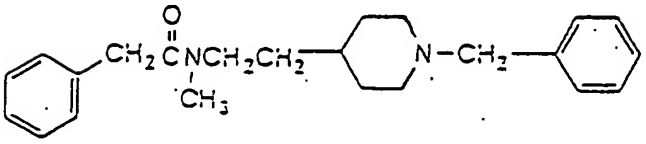


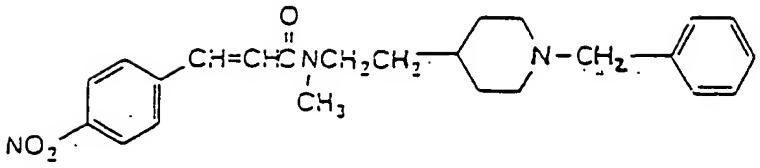


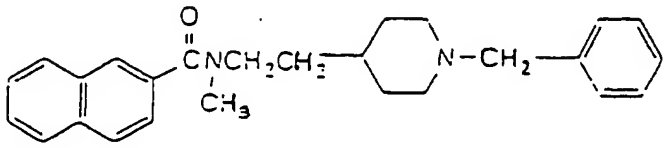




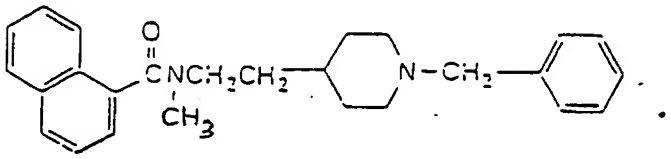








and



[0015] According to a third aspect, the present invention provides a cyclic amine compound or a pharmacologically acceptable salt thereof, which is:

Isopropyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-{2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-quinoxalinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-2-quinoxalinecarboxamide,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorocinnamide,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamide,
N-Methyl-N-[2-(1-adamanthanemethylpiperidin-4-yl)ethyl] benzamide,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamide,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanone,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamide,
Ethyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorobenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamide,
N-[2-(1-Furfrylpiperidin-4-yl)ethyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl nicotinamide or 4-(1-Benzylpiperidin-4-yl)propionanilide.

[0016] In addition, the invention provides a therapeutical composition which comprises a pharmacologically effective amount of any of the above defined cyclic amine compounds or a pharmacologically acceptable salt thereof and a pharmacologically acceptable carrier, and then the use of such cyclic amine compounds or salts for preparing a medicament for preventing or treating a disease due to the acetylcholinesterase activity.

[0017] A preferable definition of B is -CO-$(CH_2)_r$-.

[0018] The term C_{1-6} alkyl used in the above definitions is intended to mean a straight-chain or branched alkyl group

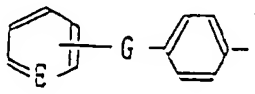
having 1 to 6 carbon atoms, and examples thereof include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl (amyl), isopentyl, neopentyl, tert-pentyl, 1-methylbutyl, 2-methylbutyl, 1,2-dimethylpropyl, hexyl, isohexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-l-methylpropyl, and 1-ethyl-2-methylpropyl groups. Among them, methyl, ethyl, propyl, isopropyl groups etc. are preferable. A methyl group is the most preferable.

[0019] Examples of the optional substituent of the phenyl group represented by J include alkyl groups having 1 to 6 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, and tert-butyl groups; alkoxy group corresponding to the above-described alkyl groups, such as methoxy and ethoxy groups; a nitro group; halogen atoms such as chlorine, bromine, and fluorine; a carboxyl group; alkoxycarbonyl groups corresponding to the above-described alkoxy groups, such as methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl, n-propoxycarbonyl, and n-butyloxycarbonyl groups; an amino group; a C_{1-6} monoalkylamino group; a C_{1-6} dialkylamino group, a carbamoyl group; acylamino groups derived from aliphatic saturated monocarboxylic acids having 1 to 6 carbon atoms, such as acetylamino; propionylamino, butyrylamino, isobutyrylamino, valerylamino, and pivaloylamino groups;

a cyclohexyloxycarbonyl group; C_{1-6} alkylaminocarbonyl groups such as methylaminocarbonyl and ethylaminocarbonyl groups; C_{1-6} alkylcarbonyloxy groups corresponding to the above-defined alkyl groups, such as methylcarbonyloxy, ethylcarbonyloxy, and n-propylcarbonyloxy groups; halogenated C_{1-6} alkyl groups including a trifluoromethyl group; a hydroxyl group; a formyl group; and C_{1-6} alkoxy C_{1-6} alkyl groups such as ethoxymethyl, methoxymethyl, and methoxyethyl groups.

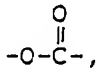
[0020] The substituent may be one to three of them which may be the same or different.

[0021] Further, J may represent:

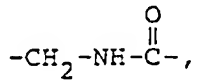


wherein G is a group represented by the formula

a group represented by the formula

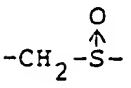


a group represented by the formula -O-, a group represented by the formula



a group represented by the formula $-CH_2-O-$, a group represented by the formula $-CH_2-SO_2-$, a group represented by the formula

and a group represented by the formula



and E is a carbon or nitrogen atom.

[0022] Preferable examples of the substituents for the phenyl group among them include alkyl, alkoxy, nitro, halogenated alkyl, alkoxycarbonyl, formyl, hydroxyl, and alkoxy alkyl groups, halogen atoms, and benzoyl and benzylsulfonyl groups. The substituent may be two or more of them which may be the same or different.

[0023] The most preferable examples of the above-defined bridging group B include those having an amide group. Therefore, it is most preferable that any portion of J-B- has a carbonyl or amide group.

[0024] The optional substituents of the phenyl group in K are the same as those described in connection with the optional substituents of J.

[0025] Preferable examples of K include benzyl and phenethyl groups.

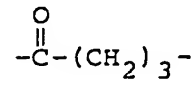
[0026] In the present invention, the term "pharmacologically acceptable salt" include those of inorganic acids, such as hydrochloride, sulfate, hydrobromide, and phosphate, and those of organic acids, such as formate, acetate, trifluoroacetate, methanesulfonate, benzenesulfonate, and toluenesulfonate. Further, when a certain kind of substituent is selected, the compound of the present invention may form, e.g., alkali metal salts such as a sodium or potassium-salt, alkaline earth metal salts such as a calcium or magnesium salt, organic amine salts such as a salt with trimethylamine, triethylamine, pyridine, picoline, dicyclohexylamine, or N,N'-dibenzylethylenediamine.

[0027] Moreover, the compounds of the present invention may have an asymmetric carbon atom depending upon the kind of the substituent and, therefore, have stereoisomers. They are, of course, within the scope of the present invention.

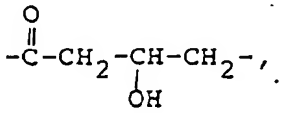
[0028] The compound of the present invention may be prepared by various processes. Representative processes for preparing the compound of the present invention will now be described.

Process A

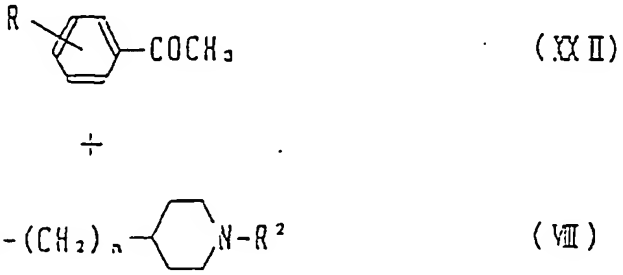
[0029] When J in the general formula (XXV) is an unsubstituted or substituted phenyl group and B is a group represented by the formula

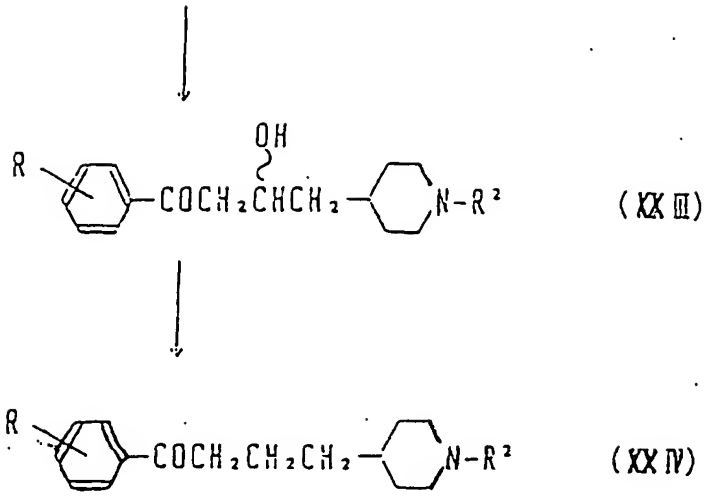


or a group represented by the formula



the compound of the present invention can be prepared also by the following process:





(XXIII)

(XXIV)

[0030] Specifically, diisopropylamine and n-butyllithium/hexane are added to a solvent such as tetrahydrofuran. In the presence of this mixture, an acetophenone represented by the general formula (XXII) is allowed to condense with a substituted N-benzyl (ω-formylalkyl)piperidine, thereby preparing a compound (XXIII). This compound is dehydrated in the presence of, e.g., p-toluenesulfonic acid in a solvent, such as toluene, followed by catalytic reduction according to an ordinary method, thereby preparing a compound (XXIV) which is one of the object compounds.

[0031] The compounds thus prepared and acid addition salts thereof represented by the general formula (I) are useful for treatment of various kinds of senile dementia, in particular senile dementia of the Alzheimer type.

[0032] The invention will be described in view of its therapeutical usefulness together with pharmacologically experimental data.

Experimental Example 1

In vitro acetylcholinesterase inhibitory action

[0033] A mouse brain homogenate was used as an acetylcholinesterase source and the esterase activity thereof was determined according to the method of Ellman et al.

Ellman, G.L., Courtney, K.D., Andres, V., and Featherstone, R.M., (1961) Biochem. Pharmacol., 7, 88-95.

[0034] Acetylthiocholine as a substrate, a sample to detect and DTNB were added to the mouse brain homogenate, followed by incubation. The amount of a yellow substance formed by the reaction between the thiocholine and DTNB was determined in the absorbance at 412 nm in terms of the acetylcholinesterase activity.

[0035] The acetylcholinesterase inhibitory activity of the sample was expressed in terms of inhibitory concentration 50% (IC_{50}).

[0036] The results are shown in Table 1.

Table 1

Compound	AChE inhibitory activity IC_{50} (μM)	Compound	AChE inhibitory activity IC_{50} (μM)
2	0.026	19	0.36
3	0.038	20	0.019
4	0.094	21	0.020
6	0.052	22	0.018
7	0.68	23	0.035
8	0.064	27	0.085
9	0.54	33	0.11
10	50	45	0.19

Table 1 (continued)

Compound	AChE inhibitory activity IC_{50} (μM)	Compound	AChE inhibitory activity IC_{50} (μM)
12	0.072	47	2.8
13	1.1		
14	24		
15	0.41		

Experimental Example 2

Ex vivo acetylcholinesterase inhibitory action

[0037] A sample to detect was orally administered to rats. After one hour of the administration, the cerebral hemispheres were dissected and homogenized, followed by the determination of the acetylcholinesterase activity. The group of rats treated with physiological saline was used as the control. Inhibition of AChE by samples ex vivo was expressed in terms of inhibition percent of the control value. Results are shown in Table 2.

Experimental Example 3

Action on passive avoidance learning impairment induced by scopolamine

[0038] See Z.Bokolanecky & Jarvik:Int.J.Neuropharmacol, 6, 217-222(1967).

[0039] Male Wister rats were used as the test animal and a step-through light and dark box was used as an apparatus. A sample to detect was orally administered one hour before the training and the rats were treated with 0.5 mg/kg (i. p.) of scopolamine 30 min. before the training. In a training experiment, the animal was placed into a light room and, just after the animal had entered into a dark room, a guillotine door was closed, followed by delivery of an electric shock from the gid of the floor. After six hours, the animal was again placed into a light room for a retention experiment, and the time taken for the animal to enter the dark room was measured for evaluation of the effect of the sample.

[0040] The difference in the response time between the physiological saline administration group and the scopolamine administration group was taken as 100%, and the effect of the sample was expressed in terms of the percentage antagonism by the sample (Reverse %).

[0041] The results are shown in Table 3.

Table 2

Compd. No.	Dose (mg/kg)	AChE inhibitory action (%)
Saline		0
4	10	5
	30	14 **
	100	18 **

Table 3

Compd. No.	Dose (mg/kg)	Reverse %
2	0.25	39
	0.5	27
4	1.0	51
	2.0	30
8	0.5	37
	1.0	39
The number of animals per dose was 10 to 17.		
NE: non-effective		

[0042] The above-described pharmacological experiments revealed that the compound of the present invention had a potent acetylcholinesterase inhibitory action.

[0043] Therefore, the objects of the present invention are to provide a novel compound effective for various kinds of dementia and the sequelae of cerebrovascular diseases, to provide a process for preparing the same, and to provide a novel pharmaceutical comprising the same as an effective ingredient.

[0044] Representative compounds of the present invention (Compd. Nos. 2, 4 and 8 in the above Table 3) were applied to toxicity tests on rats. As a result, all the compounds exhibited a toxicity of 100 mg/kg or more, i.e., exhibited no serious toxicity.

[0045] The compound of the present invention is effective for treatment, prevention, remission, improvement, etc. of various kinds of senile dementia, particularly senile dementia of the Alzheimer type; cerebrovascular diseases accompanying cerebral apoplexy, e.g. cerebral hemorrhage or cerebral infarcts, cerebral arteriosclerosis, head injury, etc.; and aprosexia, disturbance of speech, hypobulia, emotional changes, recent memory disturbance, hallucinatory-paranoid syndrome, behavioral changes, etc. accompanying encephalitis, cerebral palsy, etc.

[0046] Further, the compound of the present invention has a strong and highly selective anticholinesterase action, which renders the compound of the present invention useful also as a pharmaceutical based on this kind of action.

[0047] Specifically, the compound of the present invention is effective for, for example, Huntington's chorea, Pick's disease and delayed ataxia or tardive dyskiaesia other than senile dementia of the Alzheimer type.

[0048] When the compound of the present invention is used as a pharmaceutical for these diseases, it may be orally or parenterally administered. In general, it is parenterally administered in the form of injections, such as intravenous,-subcutaneous, and intramuscular injections, suppositories, or sublingual tablets. The does will remarkably vary depending upon the symptom; age, sex, weight, and sensitivity of patients; method of administration; time and intervals of administration and properties, dispensing, and kind of pharmaceutical preparations; kind of effective ingredients, etc., so that there is no particular limitation with respect to the dose. Normally the compound may be administered in a dose of about 0.1 to 300 mg, preferably 1 to 100 mg, per day per adult, ordinarily in one to four portions.

[0049] Pharmaceutical preparations in the dosage form of, e.g., injections, suppositories, sublingual tablets, tablets, and capsules are prepared according to a method which is commonly accepted in the art.

[0050] In preparing injections, the effective ingredient is blended, if necessary, with a pH modifier, a buffer, a suspending agent, a solubilizing agent, a stabilizer, a tonicity agent, a preservative, etc., followed by preparation of an intravenous, subcutaneous, or intramuscular injection according to an ordinary method. In this case, if necessary, it is possible to lyophilize these preparations according to an ordinary method.

[0051] Examples of the suspending agents include methylcellulose, Polysorbate 80, hydroxyethylcellulose, acacia, powdered tragacanth, sodium carboxymethylcellulose, and polyoxyethylene sorbitan monolaurate.

[0052] Examples of the solubilizing agent include polyoxyethylene hydrogenated castor oil, Polysorbate 80, nicotinamide, polyoxyethylene sorbitan monolaurate, Macrogol, and an ethyl ester of castor oil fatty acid.

[0053] Examples of the stabilizer include sodium sulfite, sodium metasulfite, and ether, and examples of the preservative include methyl p-hydroxybenzoate, ethyl p-hydroxybenzoate, sorbic acid, phenol, cresol, and chlorocresol.

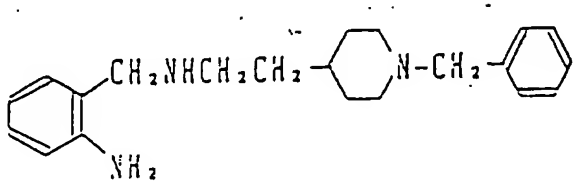
[Examples]

[0054] The present invention will now be described in more detail with reference to the following Examples. It is needless to say that the technical scope of the invention of the present invention is not limited

Example 1

4-[N-(o-Aminobenzyl)ethyl]-1-benzylpiperidine

[0055]



[0056] 30 g of 2-nitrobenzaldehyde, 21.4 g of 1-benzyl-4-aminoethylpiperidine, and 100 mℓ of methanol were stirred in a nitrogen stream at room temperature for 3 hr. -The resulting reaction mixture was cooled with ice, and a solution

of 16 g of sodium borohydride in 30 mℓ of MeOH was dropwise added thereto. The reaction was allowed to proceed at room temperature for an additional 1 hr. The reaction mixture was poured into water, extracted with methyl chloride, extracted three times with 150 mℓ of 10% hydrochloric acid, and washed with methylene chloride. Sodium carbonate was added to the water phase to adjust a pH value to 10, followed by extraction with methylene chloride. The.extract was dried over anhydrous magnesium sulfate, and the solvent was distilled off in vacuo, thereby preparing 28.4 g of 1-benzyl-4-[N-(o-nitrobenzyl)ethyl]piperidine.

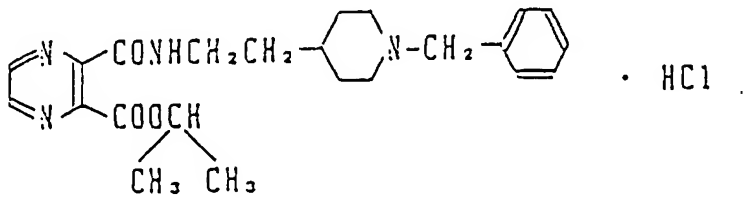
[0057] This compound was dissolved in 100 mℓ of methanol and hydrogenated in the presence of 3 g of 10% palladium-carbon (hydrous) at a pressure of 4 kg/cm^2, thereby preparing 25.6 of the title compound.

- molecular formula; $C_{21}H_{29}N_3$
- ^{1}H—NMR($CDCl_3$) δ ; 1.0 ~2.1 (9H, m), 2.64 (2H, t), 2.90 (2H, m), 3.47 (2H, s), 6.65 (2H, m), 7.02 (2H, m), 7.30 (5H, s)

Example 2

Isopropyl 3-[[4'-(1'-benzylpiperidine)propionyl]amino]-2-pyrazinecarboxylate hydrochloride

[0058]



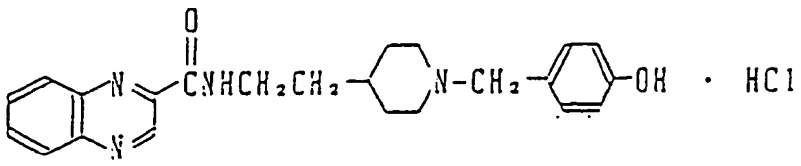
[0059] 18 g of 2,3-pyrazinecarboxylic anhydride was added to 200 mℓ of isopropyl alcohol, and the mixture was refluxed for 1 hr. Thereafter, the alcohol was distilled off therefrom. The resulting solid was dissolved in THF, and 30.6 g of 4-(2-aminoethyl)benzylpiperidine and 21 g of 1-hydroxybenzotriazole were added thereto. The mixture was stirred while cooling, and 29.7 g of DCC was added to the mixture, followed by a reaction at room temperature overnight. The reaction mixture was filtered and THF was distilled off from the filtrate, followed by addition of methylene chloride. The mixture was washed with an aqueous saturated potassium carbonate solution and then with a saline solution and dried. The solvent was distilled off therefrom. The residue was purified by making use of a silica gel column. The resulting crystal was recrystallized from ether-hexane, thereby preparing 8.81 g of a white crystal of the object compound. A hydrochloride of the compound was prepared by an ordinary method.

· elementary analysis: $C_{23}H_{30}N_4O_3$ · HCl ·I/2H_2O			
	C	H	N
calculated (%)	60.58	7.07	12.29
found (%)	60.54	7.00	12.29

Example 3

N-[4'-(1'-(p-Hydroxybenzyl)piperidine)ethyl]-2-quinoxalinecarboxylic amide hydrochloride

[0060]



[0061] 2 g of 2-quinoxalinecarboxylic acid chloride was reacted with 2.52 g of 1-(p-methoxybenzyl)-4-piperidineethylamine in the presence of 2 g of triethylamine in THF at room temperature. The reaction mixture was post-treated by an ordinary method and purified by column chromatography, thereby preparing 2.5 g of N-[4'-(1'-(p-methoxybenzyl) piperidine)ethyl]-2-quinoxalinecarboxylic amide.

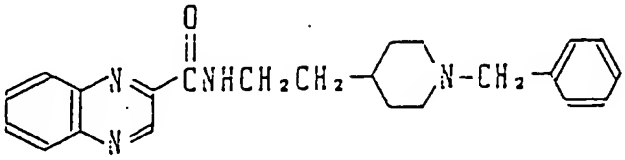
[0062] This compound was dissolved in 1 g of methylene chloride and reacted with BBr_3 for demethylation. The product was purified by column chromatography, thereby preparing 0.3 g of a product. A hydrochloride of the product was prepared to obtain 0.2 g of a creamy crystal.

- molecular formula; $C_{23}H_{26}N_4O_2 \cdot HCl$
- ^{1}H-NMR($CDCl_3$) δ ; 1.08~1.92 (9H,m), 2.84 ~3.18 (2H, m), 3.24~3.64 (2H, m), 3.52 (2H, s), 6.60 (2H, d), 7.05 (2H, d) , 7.17 (2H, s), 7.64~8.14 (4H, m), 9.53 (1H, m)

Example 4

N-[4'-(1'-Benzylpiperidyl)ethyl]-2-quinoxalinecarboxylic amide

[0063]



[0064] 40 g of 2-quinoxaloyl chloride was added to a mixture of 4.6 g of 1-benzyl-4-aminoethylpiperidine, 50 mℓ of pyridine,. and 4-dimethylaminopyridine while stirring the mixture at room temperature, followed by a reaction for 3 hr. Thereafter, the reaction mixture was poured into water, extracted with methylene chloride, and dried over anhydrous magnesium sulfate. The solvent was distilled off therefrom.

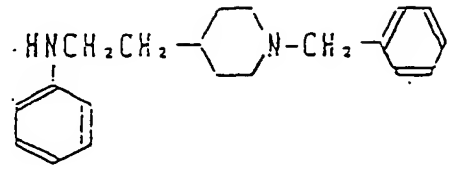
[0065] The residue was purified by silica gel chromatography (5% MeOH-$CH_2C\ell_2$) and recrystallized from ethyl acetate, thereby preparing 3.0 g of the title compound.

- molecular formula; $C_{23}H_{26}N_4O_2 \cdot HCl$
- ^{1}H-NMR($CDCl_3$) δ ; 1.16 ~2.20 (9H, m),, 2.76 ~3.04(2H, m), 3.49 (2H, s), 3.48 ~3.68 (2H, t), 7.13~7.40 (5H, m), 7.70 ~8.26 (4H,m), 9.64(1H, s)

Example 5

1-Benzyl-4-(N'-phenylaminoethyl)piperidine

[0066]



[0067] 47 g of 4-(N-benzoylpiperidyl) acetate, 8 mℓ of thionyl chloride, and 20 mℓ of benzene were heated under reflux for 2 hr. Thereafter, the solvent was distilled off in vacuo.

[0068] The residue was dissolved in 20 mℓ of THF. The resulting solution was dropwise added to a mixture of 1.86 g of aniline, 10 g of triethylamine, and 30 mℓ of THF while cooling the mixture with ice and, at the same time, stirring the mixture, followed by a reaction at room temperature for about 11 hr. The reaction mixture was poured into water and extracted with methylene chloride. The extract was washed with a saturated saline solution and dried over magnesium sulfate. The solvent was distilled off in vacuo. The residue was purified by silica gel chromatography (5% MeOH in $CH_2C\ell_2$) to prepare 0.9 g of 4-(N-benzoylpiperidyl)acetanilide.

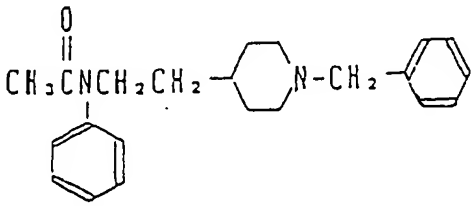
[0069] 0.9 g of 4-(N-benzoylpiperidyl)acetanilide was dissolved in 10 mℓ of THF. A solution of 0.38 g of lithium aluminum hydride in 30 mℓ of THF was dropwise added to the resulting solution while cooling and stirring the solution. The mixture was heated under reflux for additional 1 hr. After the completion of the reaction, water was added thereto. The resulting precipitate was removed by filtration. The filtrate was extracted with ethyl acetate, washed with a saturated saline solution, and dried over anhydrous magnesium sulfate. The solvent was distilled off in vacuo to prepare 0.7 of l-benzyl-4-(N'-phenylaminoethyl)-piperidine.

- molecular formula; $C_{20}H_{26}N_2$
- ^{1}H—NMR ($CDCl_3$) δ ; 1.0 ~2.2 (9H, m), 2. 85 (2H, m), 3.10 (2H, t), 3.44 (2H, s), 3.7 (1H, bs), 6.4 ~6.8 (3H, m), 7.0 ~7.4 (7H, m)

Example 6

N-[4'-(1'-Benzylpiperidyl)ethyl]acetanilide

[0070]



[0071] 0.4 g of acetyl chloride was dropwise added to a mixture of 0.7 g of 1-benzyl-4-(N'-phenylaminoethyl)piperidine, 2.0 g of triethylamine, and 20 mℓ of THF while cooling the mixture with ice under stirring.

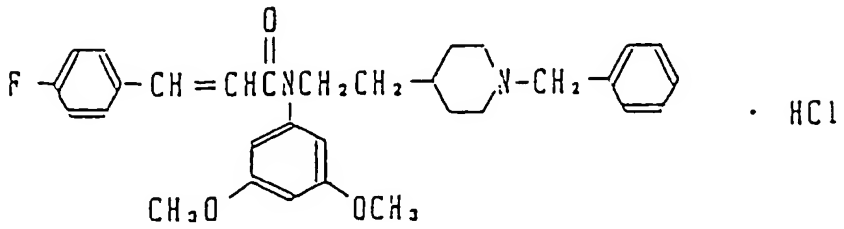
[0072] The reaction was allowed to proceed at room temperature for 3 hr, and 20 mℓ of water was added thereto, followed by extraction with methylene chloride. The extract was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The solvent was distilled off therefrom in vacuo. The residue was purified by column chromatography (5% MeOH in $CH_2C\ell_2$), thereby preparing the title compound.

- molecular formula; $C_{23}H_{28}N_2O$
- ^{1}H-NMR($CDCl_3$) δ ; 1.0 ~ 2.1 (12H, m), 2.6 ~3.0(2H,m), 3.39 (2H, s), 3.67 (2H, t), 6.9 ~7.5(10H, m)

Example 7

N-(3'5'-Dimethoxyphenyl)-N-[4'-(1'-benzylpiperidyl)ethyl]-4-fluorocinnamamide hydrichloride

[0073]



[0074] 0.51 g of p-fluorocinnamoyl chloride was added to a mixture of 1.0 g of l-benzyl-4-[N'-(3',5'-dimethoxyphenyl) aminoethyl]piperidine, 2.0 g of triethylamine, and 20 mℓ of THF while cooling the mixture with ice under stirring. The reaction was allowed to proceed at room temperature for 2 hr. Thereafter the reaction mixture was poured into water, extracted with ethyl acetate, washed with a saturated saline solution, and dried over anhydrous magnesium sulfate. The solvent was distilled off therefrom in vacuo.

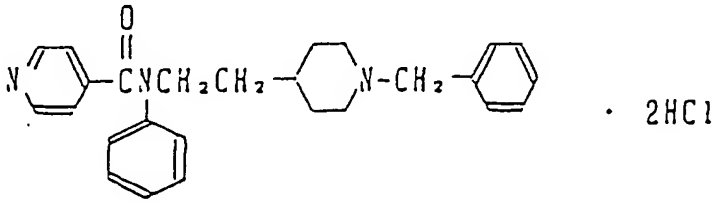
[0075] The residue was purified by silica gel chromatography (5% MeOH in $CH_2C\ell_2$). A hydrochloride of the product was prepared by an ordinary method, thereby obtaining 0.9 g of the title compound.

- molecular formula; $C_{31}H_{35}N_2O_3F \cdot HCl$
- ^1H—NMR ($CDCl_3$) δ ; 1.1 ~2.1(9H, m), 2.7 ~3.0(2H, bd), 3.51(2H, s), 3.83 (8H, m), 6.1 ~6.4 (4H, m), 6.9 ~7.8 (10H, m)

Example 8

N-[4'-(1'-Benzylpiperidine)ethyl]-N-phenylnicotinamid dihydrochloride

[0076]



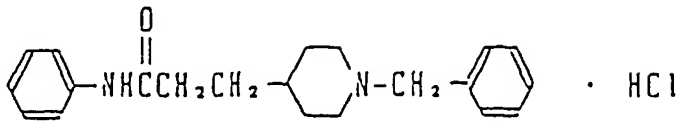
[0077] 0.70 g of N-[4'-(1'-benzylpiperidine)ethyl]aniline and a catalytic amount of 4-(N,N-dimethylamino)pyridine were dissolved in 30 mℓ of pyridine. The resulting solution was stirred while cooling it with ice. 0.85 g of isonicotinoyl chloride was added thereto, followed by stirring for 3.5 hr. The solvent was distilled off in vacuo. The residue was purified by making use of a silica gel column. A dihydrochloride of the purified product was prepared by an ordinary method. Thus there was obtained 0.75 g of a pale yellow amorphous substance (yield: 73.0%).

- molecular formula; $C_{26}H_{29}N_3O \cdot 2HCl$
- ^1H—NMR($CDCl_3$) δ ; 1.13~2.01(9H, m), 2.81 (2H, bd), 3.44 (2H, s), 3.88 (2H, bt) , 6.84~7.26 (12H, m), 8.31(2H, d)

Example 9

4-(1-Benzylpiperidine)propananilide hydrochloride

[0078]



[0079] 0.5 g of aniline and 1 g of triethylamine were dissolved in THF. 1 g of 4-(1-benzylpiperidine)propionyl chloride was dropwise added to the resulting solution while stirring the solution, followed by a reaction at room temperature for 5 hr. Thereafter the solvent was distilled off and methylene chloride was added to the residue. The resulting solution was washed with water and dried over $MgSO_4$. The solvent was again distilled off and the residue was purified by making use of a silica gel column, thereby preparing the object compound in the form of oleaginous matter. A chloride of this compound was prepared by an ordinary method, thereby obtaining 0.14 g of a white crystal.

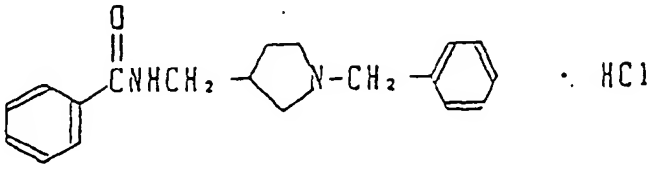
- m.p. (°C): 197.5-198°C

· elementary analysis: $C_{21}H_{26}N_2C \cdot HCl$			
	C	H	N
calculated (%)	70.28	7.58	7.81
found (%)	70.50	7.58	7.83

Example 10

N-[3'-(1'-Benzylpyrrolidine)methyl]benzamide hydrochloride

[0080]



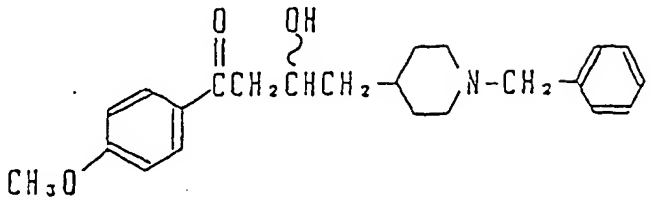
[0081] 0.74 g of benzyl chloride was reacted with 1 g of 3-(2'-aminomethyl)benzylpyrrolidine in the presence of 1.5 g of triethylamine in THF at room temperature while stirring the reaction system. The reaction mixture was.post-treated by an ordinary method and purified by column chromatography, thereby preparing 0.32 g of the object compound. A hydrochloride of the compound was prepared by an ordinary method.

- molecular formula; $C_{19}H_{22}N_2O \cdot HCl$
- ^1H-NMR($CDCl_3$) δ ; 1. 48 ~3. 08 (7H, m), 3.44 (2H, d), 3.62 (2 H, d), 7.04~7.88 (10H, m)

Example 11

4-[4'-(N-Benzyl)piperidyl]-3-hydroxy-p-methoxy-butyrophenone

[0082]



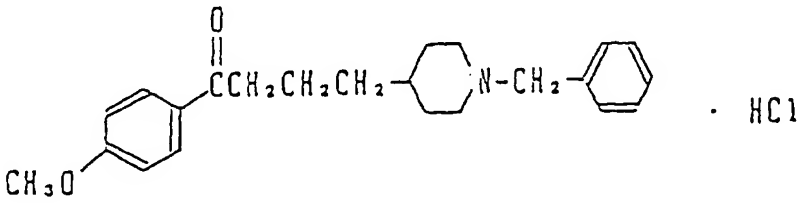
[0083] 2 mℓ of diisopropylamine was added to 7 mℓ of THF in a nitrogen stream. 7.6 mℓ of a 1.6 M solution of n-butyllithium in hexane was added thereto at 0°C. The mixture was stirred for 10 min and then cooled to -78°C. A solution of 1.65 g of p-methoxyacetophenone in 10 mℓ of THF was added thereto, and the mixture was stirred for 20 min. Further, a solution of 2.4 g of 1-benzyl-4-piperidinecarboaldehyde in 10 mℓ of THF was added thereto, and the mixture was stirred for 10 min. An aqueous 1% ammonium chloride solution was added to the reaction mixture, followed by extraction with methylene chloride. The extract was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The solvent was distilled off in vacuo. The residue was purified by silica gel column chromatography (5% MeOH-$CH_2C\ell_2$), thereby preparing 2.0 g of the title compound.

- molecular formula; $C_{23}H_{29}NO_3$
- ^{1}H-NMR($CDCl_3$) δ ; 1.0 ~2.2(9H,m), 2.6 ~3.4(5H,m), 3.43 (2H, s), 3.81 (3H, s), 4.1(1H), 6.83(2H, d), 7.17 (5H, s), 7.82 (2H, d)

Example 12

4-[4'-N-Benzyl)piperidyl]-p-methoxybutyrophenone hydrochloride

[0084]



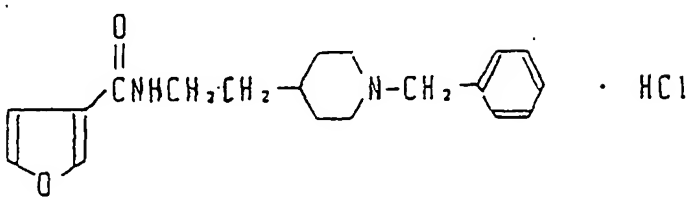
[0085] 0.54 g of 4-[4'-(N-benzyl)piperidyl]-3-hydroxy-p-methoxybutyrophenone, 0.1 g of p-toluenesulfonic acid, and 30 mℓ of toluene were heated under reflux for 5 hr by making use of a Dean-Stark reflux condenser. After the completion of the reaction, the reaction mixture was poured into an aqueous potassium carbonate solution, extracted with methylene chloride, and dried over anhydrous magnesium sulfate. The solvent was distilled off in vacuo. The residue was purified by column chromatography (5% MeOH-$CH_2C\ell_2$) to prepare 0.45 g of 1-benzyl-4-[4-(p-methoxyphenyl)-4-oxobutyl]piperidine. This compound was dissolved in 20 mℓ of MeOH and 40 mg of 10% palladium-carbon (anhydrous) was added thereto to effect hydrogenation at room temperature under atmospheric pressure for 1.5 hr. The insolubles were filtered off, and the solvent was distilled off in vacuo. A hydrochloride of the product was prepared by an ordinary method. The hydrochloride was recrystallized from MeOH-IPE, thereby preparing 0.2 g of the title compound.

- molecular formula; $C_{22}H_{29}NO_2$·HCl
- ^{1}H—NMR($CDCl_3$) δ ; 1.4 ~2.3(11H, m), 2.4 ~2.7(2H, m), 2.95(2H, t), 3.55(2H, s), 3.87(3H,s), 6.93(2H, d), 7.1 ~7.5(5H, m), 7.94(2H, d)

Example 13

N-[4'-(1'-Benzylpiperidine)ethyl]-3-furancarboxylic amide hydrochloride

[0086]



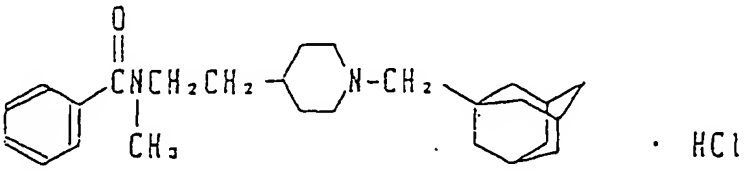
[0087] 1.64 g of 4-(2-aminoethyl)-1-benzylpiperidine and 2.67 g of potassium carbonate were added to a mixture comprising 40 mℓ of chloroform and 40 mℓ of water. The mixture was stirred for 1 hr while cooling it with ice. The organic phase was separated, washed with a saturated saline solution, and dried over magnesium sulfate. The solvent was distilled off in vacuo and the residue was purified by making use of a silica gel column. A hydrochloride of the product was prepared by an ordinary method, thereby obtaining 1.60 g of the title compound in the form of a pale yellow amorphous substance (yield: 61.1%).

- molecular formula; $C_{19}H_{24}N_2O_2 \cdot HCl$
- ^{1}H-NMR($CDCl_3$) δ ; 1.47~2.10(9H,m), 2.81 (2H, bd), 3.25~3.47(4H,m), 5.80(1H, bs), 6.51(1H, dd), 7.15~7.19 (6H,m), 7.82(1H, dd)

Example 14

N-Methyl-N-[4'-(1'-benzylpiperidine)ethyl]benzamide hydrochloride

[0088]



[0089] 0.18 g of sodium hydride was suspended in 2 mℓ of tetrahydrofuran (THF). The suspension was stirred while cooling it with ice. A solution of 1.45 g of N-[4'-(1'-benzylpiperidine)ethyl]benzamide dissolved in 5 mℓ of THF was dropwise added thereto. The mixture was stirred at room temperature for 1 hr and again cooled with ice. 0.36 mℓ of methyl iodide was added thereto, followed by stirring at room temperature overnight. The reaction mixture was poured into ice/water, extracted with chloroform while conducting salting out, washed with a saturated saline solution, and dried over magnesium sulfate. The solvent was distilled off in vacuo and the residue was purified by silica gel chromatography. Thus there was prepared 0.60 g of yellow oleaginous matter (yield: 47.0%).

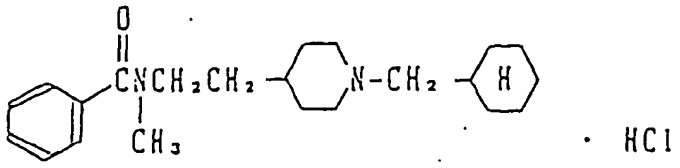
[0090] The starting material (0.22 g) remaining unmethylated was recovered (recovery: 15.2%). A hydrochloride of the obtained oleaginous matter was prepared by an ordinary method, thereby obtaining 0.52 g of the title compound in the form of a yellow amorphous substance (yield: 37.6%).

- molecular formula; $C_{26}H_{38}N_2O \cdot HCl$
- ^{1}H-NMR($CDCl_3$) δ ; 0.92~3.60(63H, m), 7.29(5H, s)

Example 15

N-[4'-(1'-Cyclohexylmethylpiperidyl)ethyl]-N-methylbenzamide hydrochloride

[0091]



[0092] 0.6 g of N-methyl-N-(4'-piperidylethyl)benzamide, 1.2 g of cyclohexyl bromide, 2.0 g of sodium bicarbonate, and 30 mℓ of methyl ethyl ketone were heated under reflux for 7 hr. After the completion of the reaction, water was added to the reaction mixture, followed by extraction with ethyl acetate. The extract was washed with a saturated saline solution and dried over anhydrous magnesium sulfate. The solvent was distilled off in vacuo. The residue was purified by silica gel chromatography (5% MeOH-$CH_2C\ell_2$), thereby preparing 0.3 g of the title compound.

- molecular formula; $C_{22}H_{34}N_2O$·HCl
- ^{1}H-NMR($CDCl_3$) δ ;0.8 ~1.1(20H, m), 1.1 ~1.6 (4H, m), 1.8 ~2.6 (5H, m), 7.4 (5H, s)

Examples 16 to 58

[0093] The compounds synthesized in the same manner as that of Examples 1 to 15 are shown in Tables 4, 6, 7 and 8.

Table 4

Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
16	· HCl	m.p. (°C): 149~150 elem. anal.: $C_{22}H_{27}NO \cdot HCl$ C H N calcd. (%) 73.83 7.88 3.91 found (%) 71.29 8.00 3.80 7/10H_2O(%) 71.31 8.00 3.78

Table 4 (cont'd)

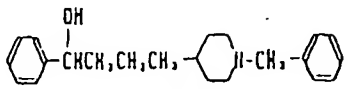
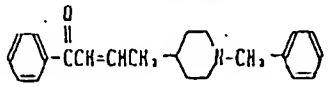
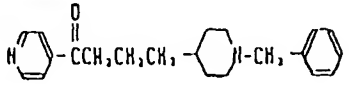
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
17	 · HCl	^{1}H-NMR($CDCl_3$) δ; 1.80∿2.03(13H,m), 2.80(3H,bd), 3.43(2H,s), 4.60(1H,t), 7.28(5H,s), 7.30(5H,s) mol. form.; $C_{22}H_{29}NO \cdot HCl$
18	 · HCl	^{1}H-NMR($CDCl_3$) δ; 1.10∿2.13(7H,m), 2.26(2H,t), 2.88(2H,bd), 3.48(2H,s), 6.72∿7.07(2H,m), 7.30(5H,s), 7.10∿8.00(5H,m) mol. form.; $C_{22}H_{25}NO \cdot HCl$
19	 · 2HCl	m.p. (°C); 176∿178 elem. anal.: $C_{21}H_{26}N_2O \cdot 2HCl$ C H N calcd. (%) 63.80 7.14 7.09 found (%) 63.13 7.43 6.88 $3/10H_2O$(%) 62.94 7.19 6.99

Table 4 (cont'd)

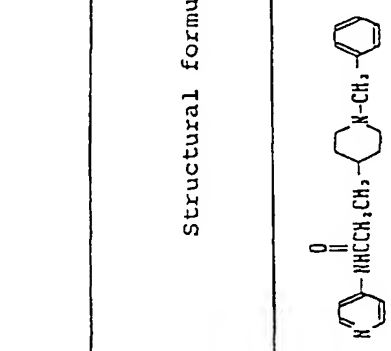
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
20	 · 2HCl	m.p. (°C); 240~240.7 elem. anal.; $C_{20}H_{25}N_3O \cdot 2HCl$ C H N calcd. (%) 66.75 7.28 11.68 found (%) 66.26 7.42 11.37 $3/20H_2O$(%) 66.25 7.31 11.59

Table 6

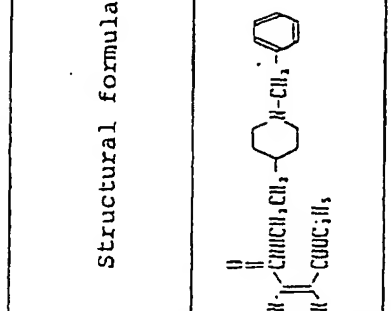
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
21		^{1}H-NMR($CDCl_3$) δ; 1.08~2.16(9H,m), 1.42(3H,t), 2.76~3.00 (2H,m), 3.32~3.62(2H,m), 3.50(2H,m), 4.53(q,2H), 7.12~7.40(5H,m), 7.48~7.72 (1H,m), 8.58(1H,d), 8.73(1H,d)

Table 7

Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
22		^{1}H-NMR($CDCl_3$)δ; 1.1~2.1(9H,m), 2.7~3.0(2H,m), 3.48(2H,s), 3.8~4.0(2H,m), 6.6~7.4(14H,m) mol. form.; $C_{27}H_{29}N_2OF\cdot HCl$
23		^{1}H-NMR($CDCl_3$)δ; 1.1~2.2(9H,m), 2.7~3.0(2H,m), 3.48(2H,s), 3.89(2H,m), 6.8~7.4(15H,m) mol. form.; $C_{27}H_{30}N_2O\cdot HCl$

Table 7 (cont'd)

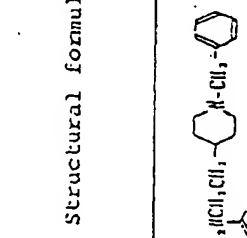
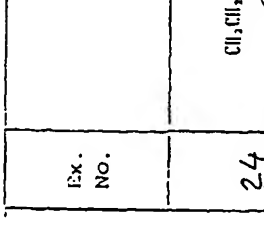
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
24		^{1}H-NMR($CDCl_3$)δ; 1.16(3H,t), 1.1~2.2(9H,m), 2.7~3.0(2H,m), 3.1~3.4(4H,m), 3.52(2H,s), 6.5~7.4(10H,m) mol. form.; $C_{22}H_{30}N_2$
25		^{1}H-NMR($CDCl_3$)δ; 1.78(3H,s), 1.0~2.1(9H,m), 2.6~3.0(2H,m), 3.43(2H,s), 3.75(2H,m), 3.73(3H,s), 6.64(4H,dd), 7.26(5H,s) mol. form.; $C_{23}H_{30}N_2O_2 \cdot HCl$
26		^{1}H-NMR($CDCl_3$)δ; 1.1~2.1(9H,m), 1.84(3H,s), 2.7~3.0(2H,m), 3.44(2H,s), 3.5~3.8(2H,m), 3.80(3H,s), 6.5~6.9(3H,m), 7.22(6H,s) mol. form.; $C_{23}H_{30}N_2O_2$
27		^{1}H-NMR($CDCl_3$)δ; 1.16~2.16(9H,m), 2.68~2.98(2H,m), 3.49(2H,s), 3.84~4.09(2H,t), 6.91~7.40 (10H,m), 8.22~8.44(2H,m), 8.62(1H,s)

Table 7 (cont'd)

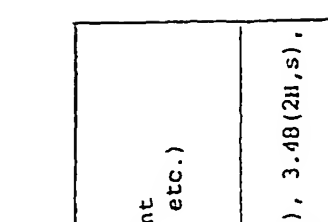
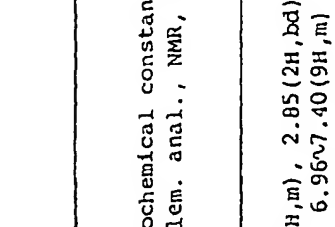
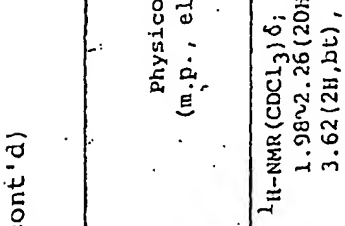
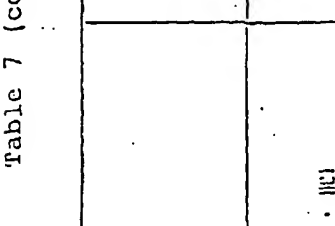
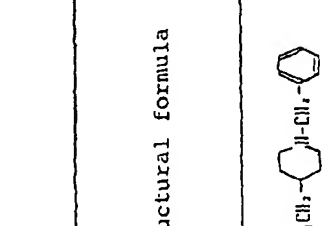
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
28	 · HCl	^{1}H-NMR(CDCl$_3$)δ; 1.98~2.26(20H,m), 2.85(2H,bd), 3.48(2H,s), 3.62(2H,bt), 6.96~7.40(9H,m) mol. form.; $C_{27}H_{36}N_2O\cdot HCl$
29	 · HCl	^{1}H-NMR(CDCl$_3$)δ; 0.90~2.10(9H,m), 2.65~2.98(2H,m), 2.83(3H,s), 3.47(2H,s), 3.52~3.92(2H,m), 7.26(5H,s), 7.26~7.43(5H,m) mol. form.; $C_{21}H_{20}N_2O_2S\cdot HCl$
30	 · HCl	^{1}H-NMR(CDCl$_3$)δ; 1.02(3H,t), 1.10~2.00(9H,m), 1.98(2H,q), 2.80(2H,bd), 3.43(2H,s), 3.55~3.80(2H,m), 6.97~7.40(5H,m), 7.20(5H,s) mol. form.; $C_{23}H_{30}N_2O\cdot HCl$
31	 · 2HCl	^{1}H-NMR(CDCl$_3$)δ; 1.0~2.1(9H,m), 2.18(6H,s), 2.6~3.0(4H,m), 3.38(2H,s), 3.4~3.8(2H,m), 6.9~7.5(10H,m) mol. form.; $C_{24}H_{33}N_3O\cdot 2HCl$
32	 · HCl	^{1}H-NMR(CDCl$_3$)δ; 1.17(3H,t), 1.1~2.1(9H,m), 2.6~2.9(2H,m), 3.40(2H,s), 3.4~3.8(2H,m), 4.08(2H,t), 7.19(10H,s) mol. form.; $C_{23}H_{30}N_2O_2\cdot HCl$

Table 7 (cont'd)

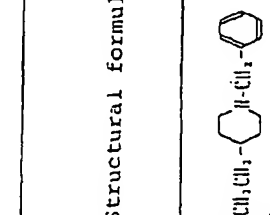
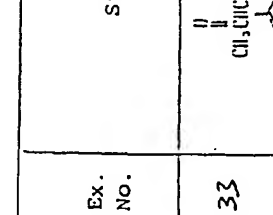
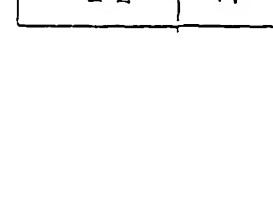
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
33		^{1}H-NMR($CDCl_3$)δ; 1.24~1.81(9H,m), 2.0(3H,s), 2.82~2.96 (2H,d), 3.54(2H,s), 3.80(2H,m), 7.18 (2H,dd), 7.36(5H,s), 8.70(2H,dd) mol. form.; $C_{21}H_{27}N_3O$
34	 · HCl	^{1}H-NMR($CDCl_3$)δ; 1.83(3H,s), 1.0~2.2(9H,m), 2.6~3.0(2H,m), 3.43(2H,s), 3.66(3H,t), 6.8~7.4(9H,m) mol. form.; $C_{22}H_{27}N_2OCl \cdot HCl$
35	 · HCl	^{1}H-NMR($CDCl_3$)δ; 1.16~2.06(9H,m), 2.83(2H,bd), 3.47(2H,s), 3.78(2H,bt), 5.42(1H,dd), 5.90(1H,dd), 6.20(1H,dd), 6.99~7.40(10H,m) mol. form.; $C_{23}H_{28}N_2O \cdot HCl$
36	· HCl	^{1}H-NMR-($CDCl_3$)δ; 1.14~2.03(12H,m), 2.83(2H,bd), 3.44(2H,s), 3.64(2H,bt), 7.00(2H,s), 7.08(2H,s), 7.22(5H,s) mol. form.; $C_{22}H_{27}FN_2O \cdot HCl$
37	· HCl	^{1}H-NMR($CDCl_3$)δ; 1.15~1.95(12H,m), 2.84(2H,bd), 3.65(2H,s), 3.67(2H,bt), 6.75~7.07(3H,m), 7.23(6H,s) mol. form.; $C_{22}H_{27}FN_2O \cdot HCl$

Table 7 (cont'd)

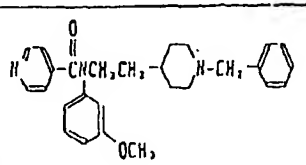
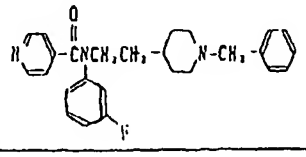
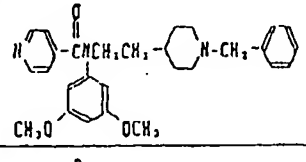
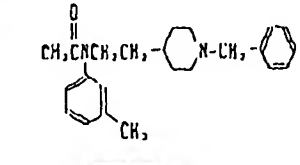
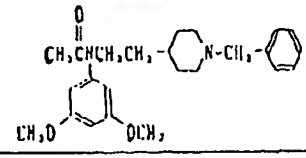
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
38	 · 2HCl	^{1}H-NMR($CDCl_3$) δ; 1.0∿2.1(9H,m), 2.6∿3.0(2H,m), 3.43(2H,s), 3.85(2H,m), 6.4∿6.7(3H,m), 6.9∿7.3(8H,m), 8.34(2H,d) mol. form.; $C_{27}H_{31}N_3O_2 \cdot 2HCl$
39	 · 2HCl	^{1}H-NMR($CDCl_3$) δ; 1.0∿2.1(9H,m), 2.6∿3.0(2H,m), 3.41(2H,s), 3.84(2H,m), 6.6∿7.2(5H,m), 7.22(5H,s), 8.37(2H,d) mol. form.; $C_{26}H_{28}N_3OF \cdot 2HCl$
40	 · 2HCl	^{1}H-NMR($CDCl_3$) δ; 1.0∿2.1(9H,m), 2.6∿3.0(2H,m), 3.43(2H,s), 3.57(6H,s), 3.83(2H,m), 6.0∿6.2(3H,m), 7.0∿7.4(7H,m), 8.35(2H,d)
41	 · HCl	^{1}H-NMR($CDCl_3$) δ; 1.77(3H,s), 1.0∿2.1(9H,m), 2.32(3H,s), 2.6∿2.9(2H,m), 3.40(2H,s), 3.63(2H,m), 6.7∿7.3(9H,m) mol. form.; $C_{28}H_{33}N_3O_3 \cdot HCl$
42	 · HCl	^{1}H-NMR($CDCl_3$) δ; 1.85(3H,s), 1.1∿2.2(9H,m), 2.6∿3.0(2H,m), 3.42(2H,s), 3.60(2H,m), 3.75(6H,s), 6.20(2H,d), 6.35(1H,m), 7.18(5H,s) mol. form.; $C_{24}H_{32}N_2O_3 \cdot HCl$

Table 7 (cont'd)

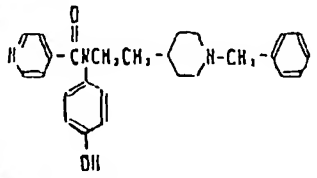
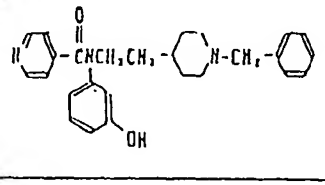
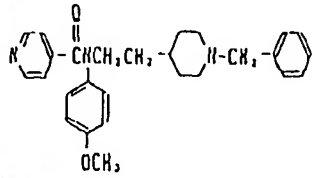
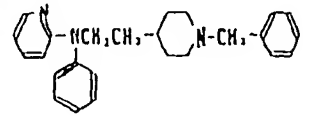
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
43	 · 2HCl	^{1}H-NMR($CDCl_3$)δ; 1.1∿2.1(9H,m), 2.6∿3.0(2H,m), 3.50(2H,s), 3.83(2H,m), 6.58(4H,dd), 7.04(2H,d), 7.19(5H,s), 8.28(2H,d) mol. form.; $C_{26}H_{29}N_3O_2 \cdot 2HCl$
44	 · 2HCl	^{1}H-NMR($CDCl_3$)δ; 1.07∿2.35(9H,m), 2.99(2H,bd), 3.62(2H,s), 3.81(2H,bt), 6.31∿6.56(3H,m), 6.84∿7.11 (3H,m), 7.25(5H,s), 8.31(2H,bs) mol. form.; $C_{26}H_{29}N_3O_2 \cdot 2HCl$
45	 · 2HCl	^{1}H-NMR($CDCl_3$)δ; 1.1∿2.1(9H,m), 2.6∿3.0(2H,m), 3.44(2H,s), 3.68(3H,m), 3.85(2H,m), 6.78(4H,dd), 7.02(2H,d), 7.23(5H,s), 8.37(2H,d) mol. form.; $C_{27}H_{31}N_3O_2 \cdot 2HCl$
46	 · 2HCl	^{1}H-NMR($CDCl_3$)δ; 7.20(11H,m), 8.05(1H,m), 1.2∿1.83(9H,m), 2.65∿2.81(2H,d), 3.4(2H,s), 3.90(2H,m), 6.20∿6.52(2H,m) mol. form.; $C_{25}H_{29}N_3 \cdot 2HCl$

Table 8

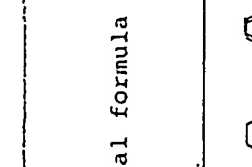
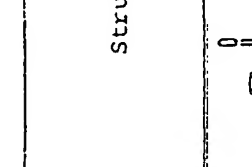
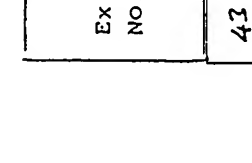
Ex. No.	Structural formula	Physicochemical constant (m.p.; elem. anal., NMR, etc.)
43		^{1}H-NMR($CDCl_3$) δ; 1.0~2.1(9H,m), 2.31(3H,s), 2.5~3.1(5H,m), 3.1~3.6(4H,m), 7.0~7.4(9H,m) mol. form.; $C_{23}H_{30}N_2O \cdot HCl$
44		^{1}H-NMR($CDCl_3$) δ; 1.0~2.2(9H,m), 2.7~3.0(2H,m), 3.29(2H,m), 3.50(2H,s), 3.81(2H,s), 5.8(1H,s), 7.25 (5H,s), 7.3~7.7(3H,m), 8.03(1H,d) mol. form.; $C_{22}H_{27}N_3O_3 \cdot HCl$
45		^{1}H-NMR($CDCl_3$) δ; 1.20~2.08(9H,m), 2.80~2.92(2H,d), 3.12 (3H,s), 3.46~3.64(4H,m), 6.42(1H,dd), 7.00(1H,dd), 7.26~7.45(6H,m) mol. form.; $C_{20}H_{26}N_2O_2 \cdot HCl$

Table 8 (cont'd)

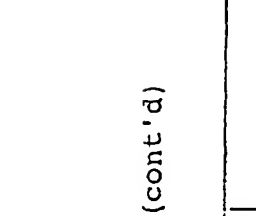
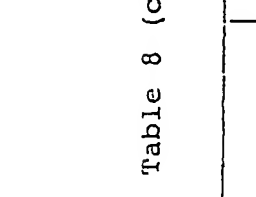
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
46		^{1}H-NMR($CDCl_3$)δ; 1.1~2.1(7H,m), 2.8~3.05(2H,m), 3.05~3.15 (2H,m), 3.49(2H,s), 5.1(1H,), 7.0~7.5 (10H,m) mol. form.; $C_{20}H_{24}N_2O_2 \cdot HCl$
47		^{1}H-NMR($CDCl_3$)δ; 1.30~2.24(9H,m), 2.86(2H,bd), 3.32~3.60 (4H,m), 6.08~6.28(2H,m), 7.20~8.02(6H,m) mol. form.; $C_{19}H_{24}N_2O_2 \cdot HCl$
48		^{1}H-NMR($CDCl_3$)δ; 1.1~2.2(9H,m), 2.8~3.1(2H,m), 3.50(4H,s), 7.30(10H,s) mol. form.; $C_{20}H_{23}NO_3 \cdot HCl$

Table 8 (cont'd)

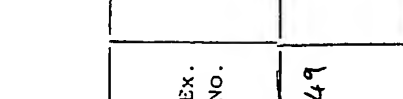
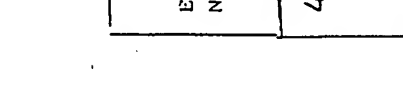
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
49		^{1}H-NMR($CDCl_3$) δ; 1.1~2.2(9H,m), 2.7~3.0(2H,m), 3.1~3.4(2H, m), 3.46(2H,s), 4.90(1H), 6.9~7.4(10H,m) mol. form.; $C_{21}H_{26}N_2O_2 \cdot HCl$
50		^{1}H-NMR($CDCl_3$) δ; 1.1~2.2(9H,m), 2.7~3.0(4H,m), 3.1~3.6 (2H,m), 3.55(2H,s), 5.5(1H), 7.30(10H,s) mol. form.; $C_{22}H_{28}N_2O \cdot HCl$
51		^{1}H-NMR($CDCl_3$) δ; 1.1~2.2(9H,m), 2.7~3.0(2H,m), 3.2~3.4 (2H,m), 3.40(2H,s), 5.9(1H), 6.39(1H,d), 7.1~7.8(11H,m) mol. form.; $C_{23}H_{28}N_2O \cdot HCl$

Table 8 (cont'd)

Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
52		^{1}H-NMR($CDCl_3$)δ; 1.0~2.1(9H,m), 2.7~3.0(2H,m), 3.48(2H,s), 4.36(2H,t), 7.0~7.7(8H,m), 7.8~8.2(2H,m) mol. form.: $C_{21}H_{25}NO_2$

Table 8 (cont'd)

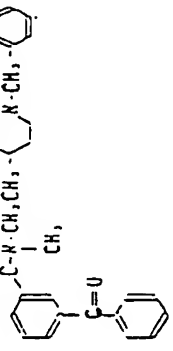
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
53		^{1}H-NMR($CDCl_3$)δ; 0.96~2.08(3H,m), 2.60~3.10(6H,m), 3.48(2H,d), 7.16~7.92(14H,m)

Table 8 (cont'd)

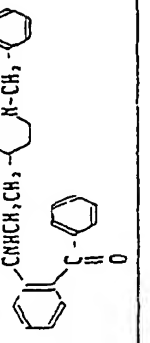
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
54	 · HCl	^{1}H-NMR($CDCl_3$) δ; 0.80~2.04(9H,m), 2.48~2.88(2H,m), 3.12~3.52(4H,m) 7.03~7.72(14H,m)

Table 8 (cont'd)

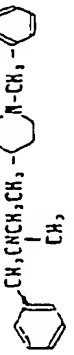
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
54	 · HCl	^{1}H-NMR($CDCl_3$) δ; 1.00~2.08(9H,m), 2.78(2H,bd), 2.88(3H,s), 3.10~3.45(2H,m), 3.43(2H,s), 3.57(2H,s), 7.22(10H,s) mol. form.; $C_{23}H_{30}N_2O \cdot HCl$

Table 8 (cont'd)

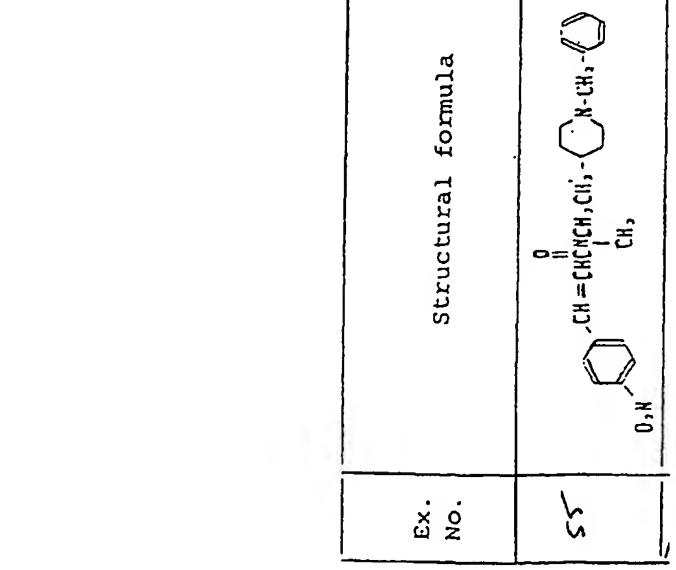
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
55		^{1}H-NMR($CDCl_3$)δ; 1.1~2.2(9H,m), 2.6~3.2(5H,m), 3.2~3.6 (4H,m), 6.8~7.1(1H,m), 7.3(5H,s), 7.5~7.8(3H,m), 8.24(2H,d) mol. form.; $C_{26}H_{29}N_3O_3 \cdot HCl$

Table 9(cont'd)

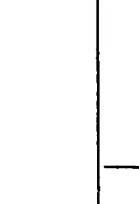
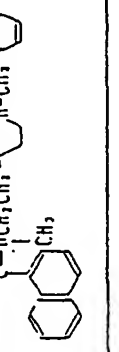
Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
56	· HCl	^{1}H-NMR($CDCl_3$)δ; 1.00~2.00(4H,m), 2.83(2H,bd), 3.24(2H,bd), 3.45(2H,s), 3.59(2H,s), 5.85(1H,bs), 7.27(5H,s), 7.77(4H,ABq) mol. form.; $C_{22}H_{27}N_3O_3 \cdot HCl$
57	 · HCl	^{1}H-NMR($CDCl_3$)δ; 1.0~2.1(9H,m), 2.6~3.2(5H,m), 3.2~3.7 (4H,m), 7.25(5H,s), 7.3~8.1(7H,m) mol. form.; $C_{26}H_{30}N_2O \cdot HCl$

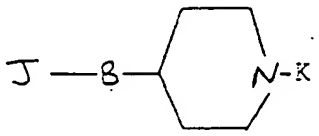
Table 8 (cont'd)

Ex. No.	Structural formula	Physicochemical constant (m.p., elem. anal., NMR, etc.)
58	 · HCl	^{1}H-NMR($CDCl_3$)δ; 0.90~1.05(9H,m), 2.70(3H,s), 3.00(2H,d), 3.22(2H,s), 3.37(1H,s), 3.46(1H,s), 7.18~7.60(9H,m), 7.78(3H,m) mol. form.: $C_{26}H_{30}N_2O \cdot HCl$

Claims

Claims for the following Contracting States : AT, BE, CH, LI, DE, FR, GB, IT, LU, NL, SE,

1. A cyclic amine compound having the following formula (XXV) or a pharmacologically acceptable salt thereof:



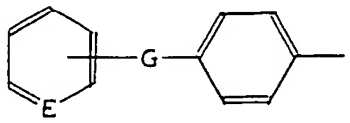
(XXV)

wherein:

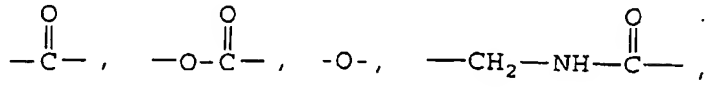
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

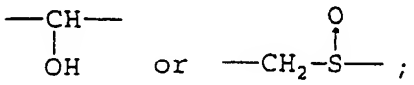
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



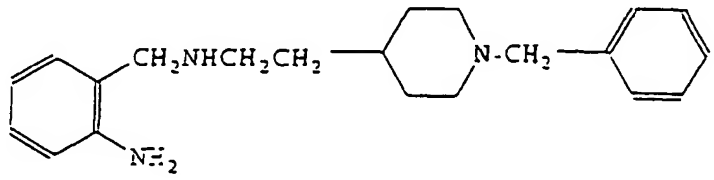
and E is a carbon or nitrogen atom;

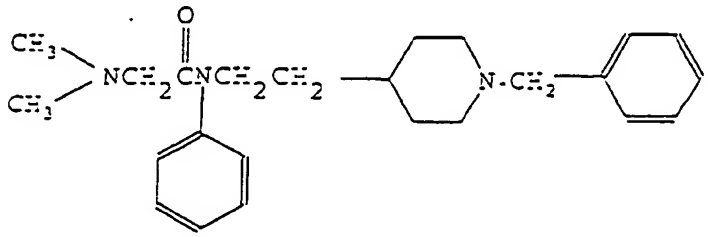
the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6 with the proviso that if B is $-NR^4-(CH_2)_r-$ then r is not zero, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

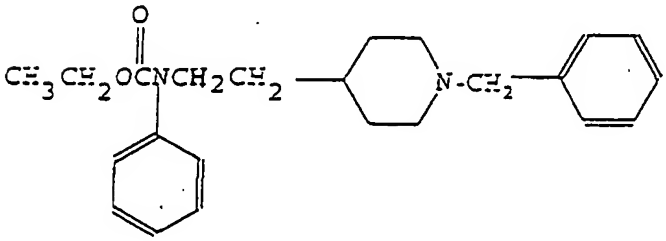
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a car-

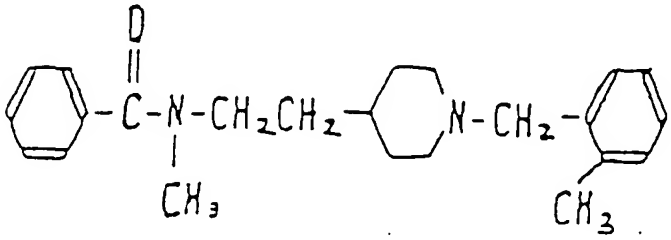
bamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

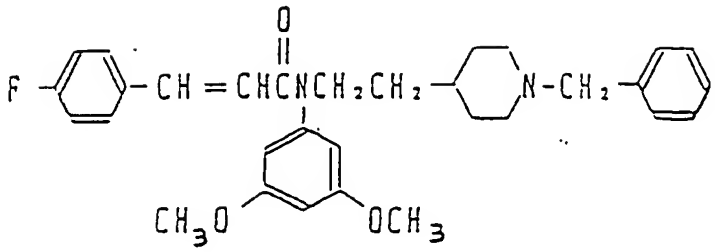
2. A cyclic amine compound of any one of the formulae :

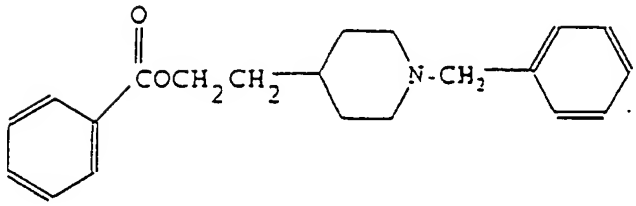


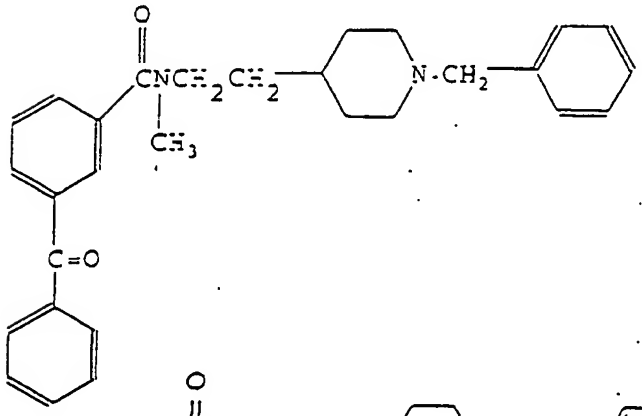


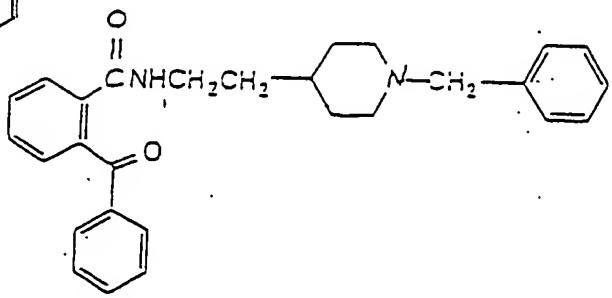


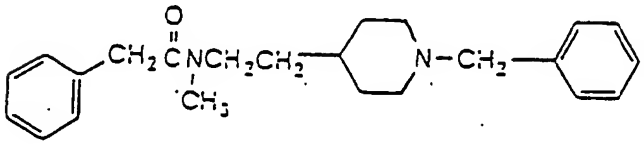


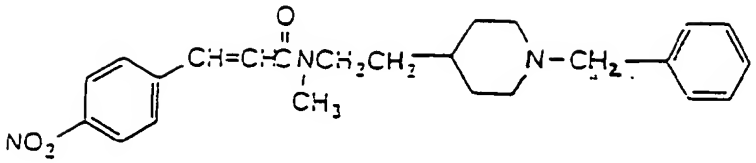


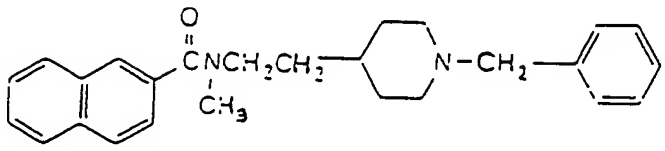




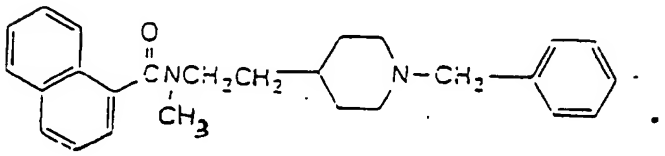








and



3. A cyclic amine compound or a pharmacologically acceptable salt thereof according to Claim 1, which is:
4-(N-Benzylpiperidin-4-yl)-(4-methoxy) butyrophenone.

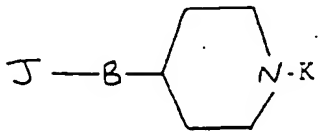
4. A cyclic amine compound or a pharmacologically acceptable salt thereof, which is:

Isopropyl 3-(N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-{2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-quinoxalinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-2-quinoxalinecarboxamide,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorocinnamide,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamide,
N-Methyl-N-[2-(1-adamanthanemethylpiperidin-4-yl)ethyl] benzamide,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamide,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanone,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamide,
Ethyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorobenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamide,
N-[2-(1-Furfrylpiperidin-4-yl)ethyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl nicotinamide or 4-(1-Benzylpiperidin-4-yl)propionanilide.

5. A therapeutical composition which comprises a pharmacologically effective amount of a cyclic amine compound as defined in any preceding Claim or a pharmacologically acceptable salt thereof and a pharmacologically acceptable carrier.

6. The use of a cyclic amine compound as defined in Claim 2, 3, 4 or having the following formula (XXV)'

or a pharmacologically acceptable salt thereof:



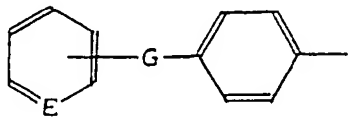
(XXV)'

wherein:

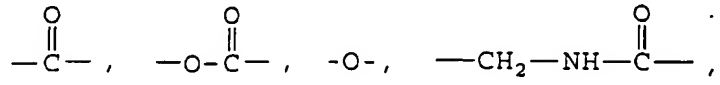
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

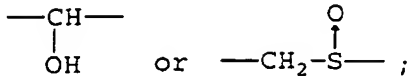
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



and E is a carbon or nitrogen atom;

the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$,$-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

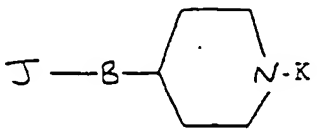
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group,

or a pharmacologically acceptable salt thereof,
for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity.

7. The use as claimed in Claim 6, wherein the medicament is effective against senile dementia.

8. The use as claimed in Claim 6, wherein the medicament is effective against senile dementia of Alzheimer type.

9. A method for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity **characterized in** the use, as an essential constituent of said agent, of a cyclic amine compound as defined in Claims 2, 3, 4, or having the following formula (XXV)' or a pharmacologically acceptable salt thereof:



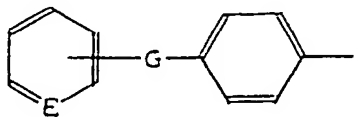
(XXV)'

wherein:

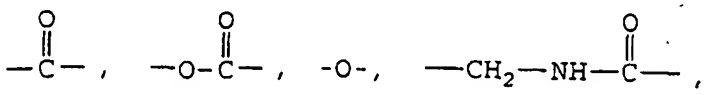
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

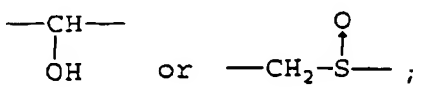
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



and E is a carbon or nitrogen atom;

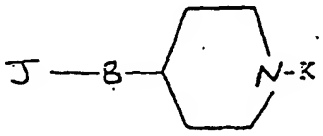
the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6, $-CO-CH=CH-CH_2-$, -CO-

CH_2-CH(OH)-CH_2-, -CH(CH_3)-CO-NH-CH_2- or -CH=CH-CO-NH-$(CH_2)_2$-; and

K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

Claims for the following Contracting States : ES, GR

1. A cyclic amine compound having the following formula (XXV) or a pharmacologically acceptable salt thereof:



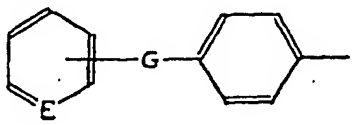
(XXV)

wherein:

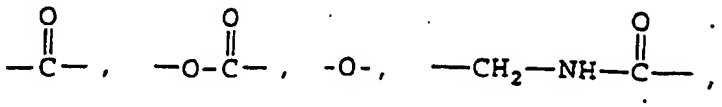
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

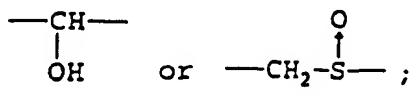
(ii)



wherein G represents



-CH_2-O-, -CH_2-SO_2-,

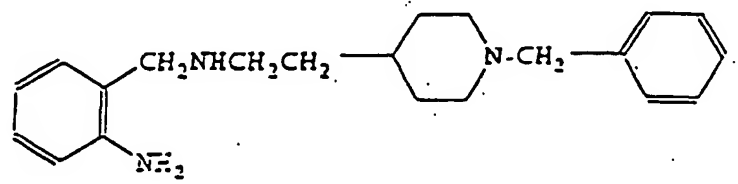


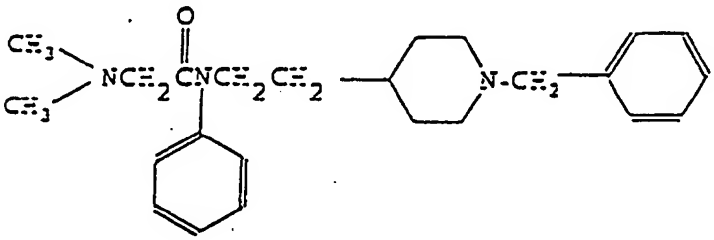
and E is a carbon or nitrogen atom;

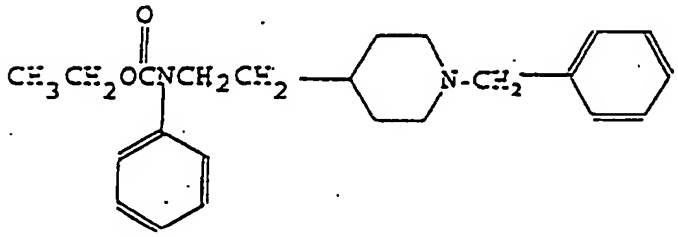
the bridging group -B- is -CO-$(CH_2)_r$-, -NR^4-$(CH_2)_r$-, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, -CH=CH-$(CH_2)_r$-, -OCOO-$(CH_2)_r$-, -OOC-NH-$(CH_2)_r$-, -CH_2-CO-NH-$(CH_2)_r$-, -$(CH_2)_2$-CO-NH-$(CH_2)_r$-, -CH(OH)-$(CH_2)_r$-, r being zero or an integer of 1 to 6 with the proviso that if B is -NR^4-$(CH_2)_r$- then r is not zero, -CO-CH=CH-CH_2-, -CO-CH_2-CH(OH)-CH_2-, -$CH(CH_3)$-CO-NH-CH_2- or -CH=CH-CO-NH-$(CH_2)_2$-; and

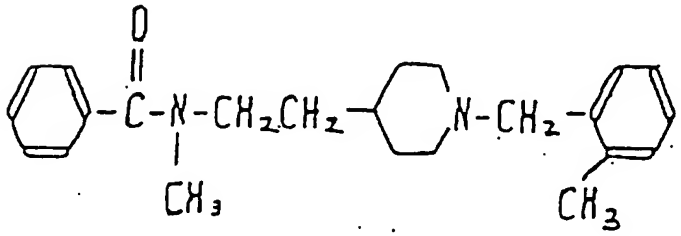
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

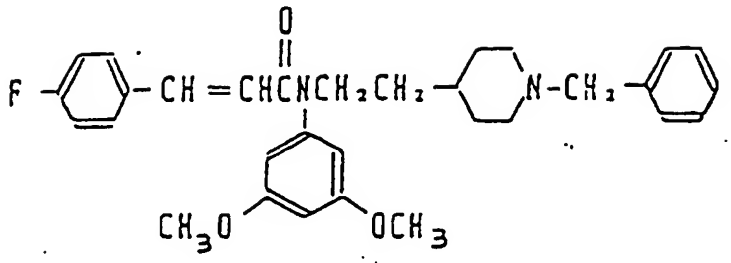
2. A cyclic amine compound of any one of the formulae:

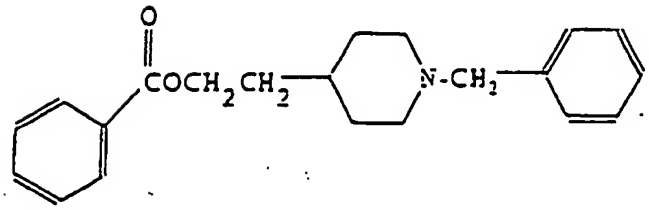


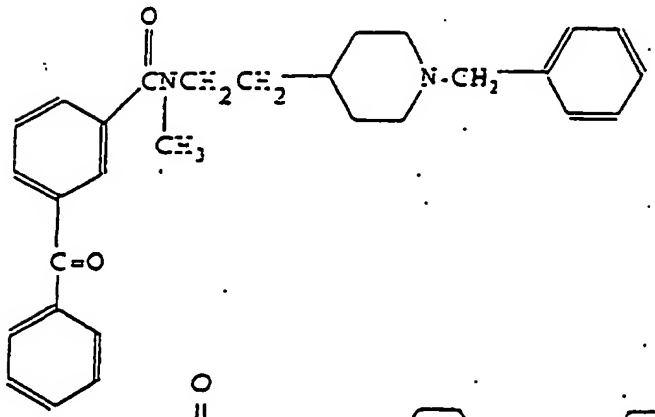


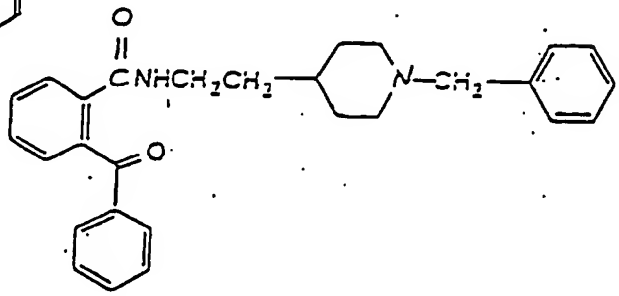


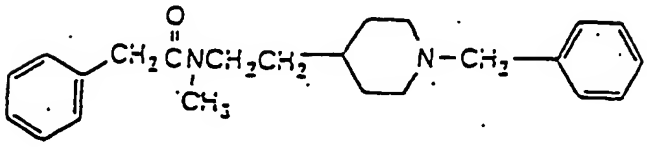


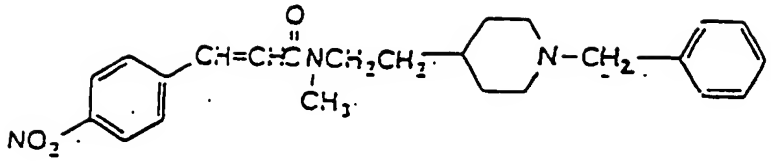


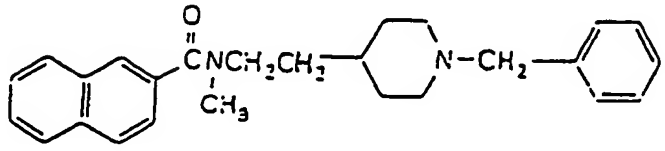




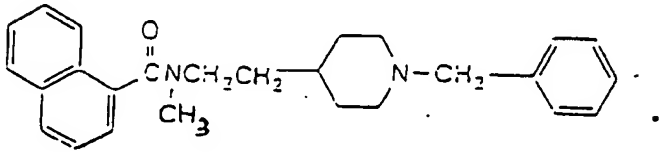








and



3. A cyclic amine compound or a pharmacologically acceptable salt thereof according to Claim 1, which is:
4-(N-Benzylpiperidin-4-yl)-(4-methoxy) butyrophenone.

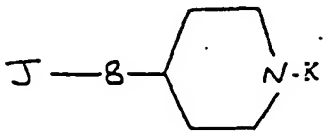
4. A cyclic amine compound or a pharmacologically acceptable salt thereof, which is:

Isopropyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-{2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-quinoxalinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-2-quinoxalinecarboxamide,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorocinnamide,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamide,
N-Methyl-N-[2-(1-adamanthanemethylpiperidin-4-yl)ethyl] benzamide,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl) ethyl]-N-methylbenzamide,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanone,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamide,
Ethyl 3-{N-[2-(1-benzylpiperidin-4-yl),ethyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorobenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamide,
N-[2-(1-Furfrylpiperidin-4-yl)ethyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl nicotinamide or 4-(1-Benzylpiperidin-4-yl)propionanilide.

5. A therapeutical composition which comprises a pharmacologically effective amount of a cyclic amine compound as defined in any preceding Claim or a pharmacologically acceptable salt thereof and a pharmacologically acceptable carrier.

6. The use of a cyclic amine compound having the following formula (XXV)'

or a pharmacologically acceptable salt thereof:



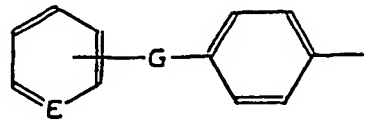
(XXV)'

wherein:

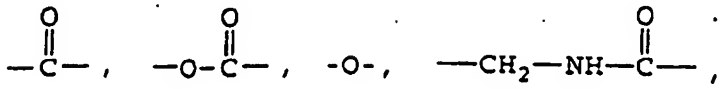
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

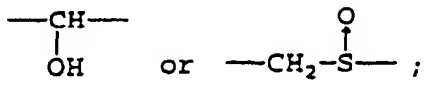
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



and E is a carbon or nitrogen atom;

the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$,$-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

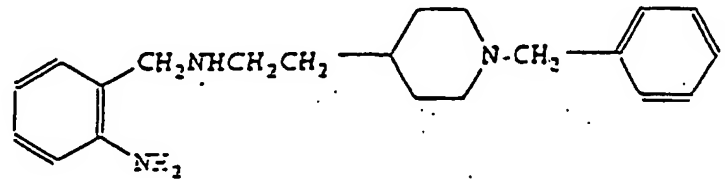
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6}

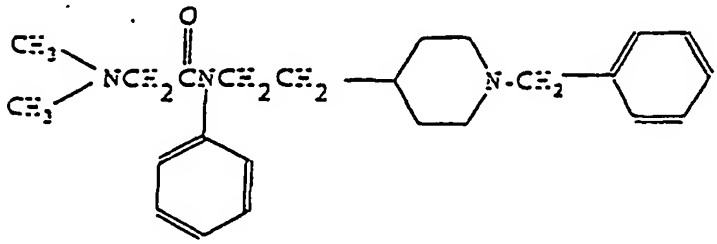
alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group,

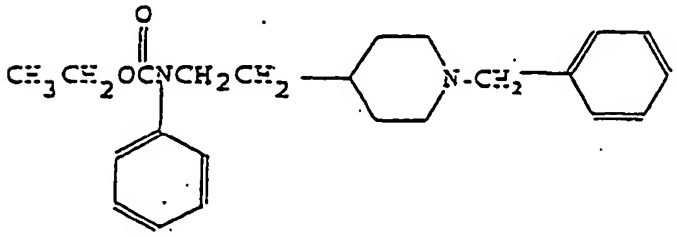
or a pharmacologically acceptable salt thereof,

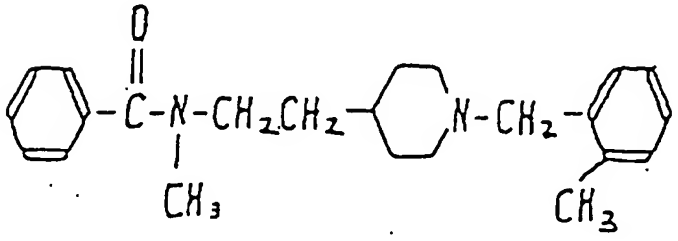
for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity.

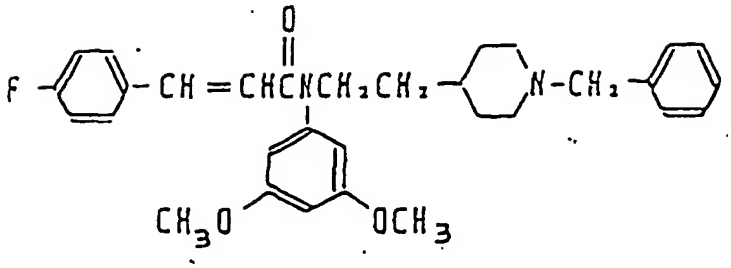
7. The use of a cyclic amino compound or a pharmaceutically acceptable salt thereof of any one of the formulae

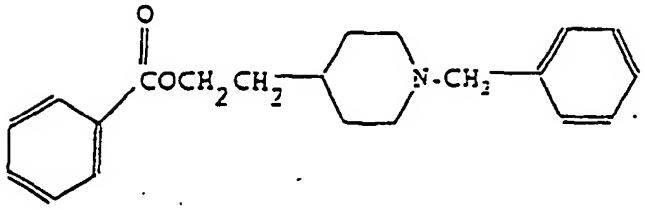


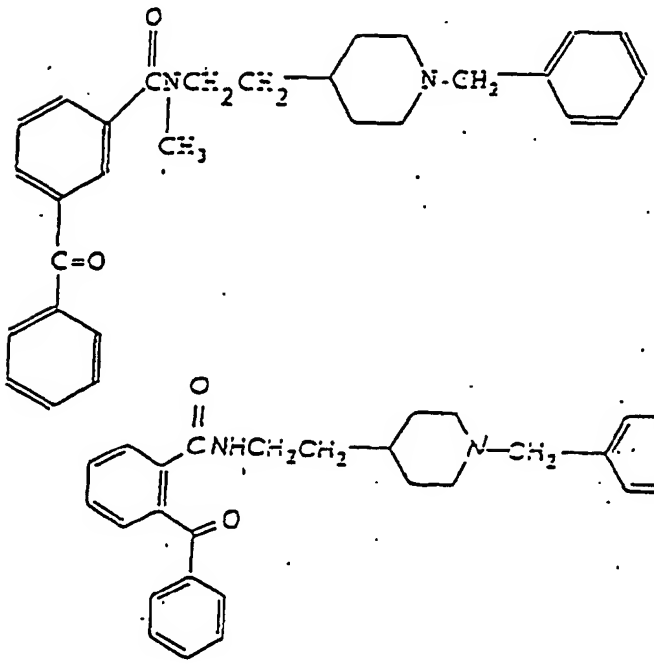


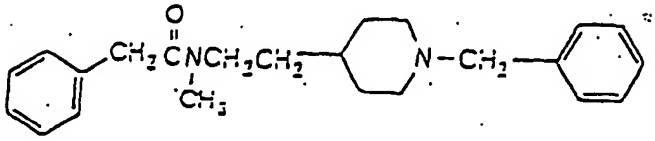


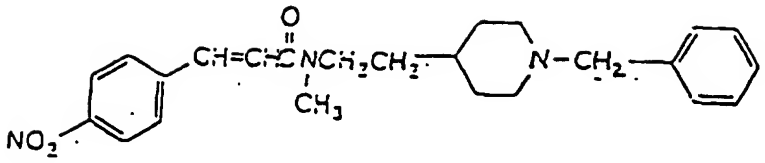


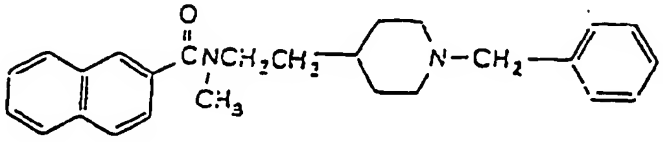




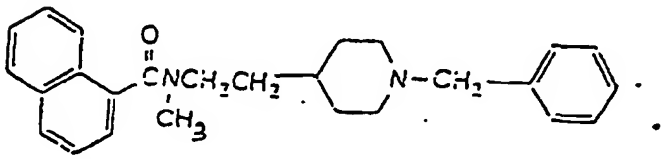








and



for preparing, a medicament for the treatment of a disease due to acetylcholinesterase activity.

8. The use according to claim 6 wherein the cyclic amine compound is 4-(N-Benzylpiperidin-4-yl)-(4-methoxy) butyrophenone.

9. The use of a cyclic amine compound or a pharmaceutically acceptable salt thereof which is

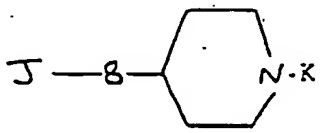
Isopropyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido)-2-pyrazinecarboxylate,
N-{2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-quinoxalinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-2-quinoxalinecarboxamide,
N- (3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl) ethyl]-4-fluorocinnamide,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamide,
N- [2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamide,
N-Methyl-N-[2-(1-adamanthanemethylpiperidin-4-yl)ethyl] benzamide,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamide,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanone,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamide,
Ethyl 3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorobenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamide,
N-[2-(1-Furfrylpiperidin-4-yl)ethyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl nicotinamide or 4-(1-Benzylpiperidin-4-yl)propionanilide.

for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity.

10. The use as claimed in any one of Claims 6 to 9, wherein the medicament is effective against senile dementia.

11. The use as claimed in any one of Claims 6 to 9, wherein the medicament is effective against senile dementia of Alzheimer type.

12. A method for preparing a medicament for the treatment of a disease due to acetylcholinesterase activity **characterized in** the use, as an essential constituent of said agent, of a cyclic amine compound as defined in Claims 7, 8, 9 or having the following formula (XXV)' or a pharmacologically acceptable salt thereof:



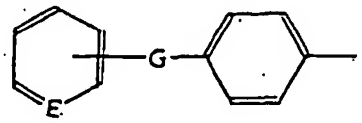
(XXV)'

wherein:

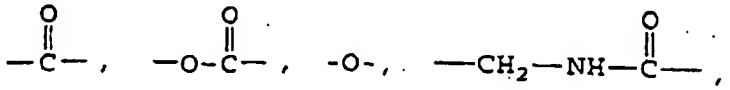
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

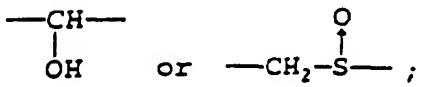
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,



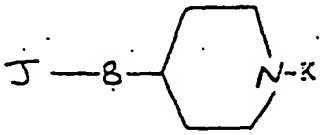
and E is a carbon or nitrogen atom;

the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a

C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

13. A process for preparing a pharmaceutical composition comprising the step of mixing a pharmaceutically acceptable carrier and a cyclic amine compound having the following formula (XXV) or a pharmacologically acceptable salt thereof:



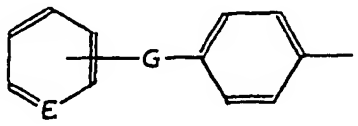
(XXV)

wherein:

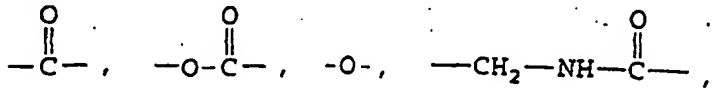
J is:

(i) a phenyl group optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group; or

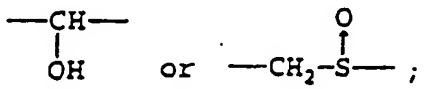
(ii)



wherein G represents



$-CH_2-O-$, $-CH_2-SO_2-$,

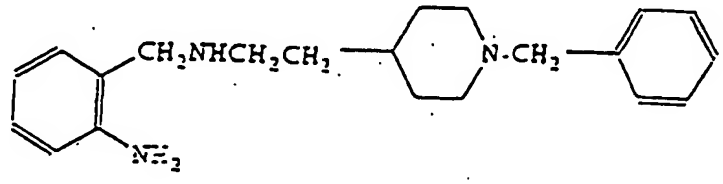


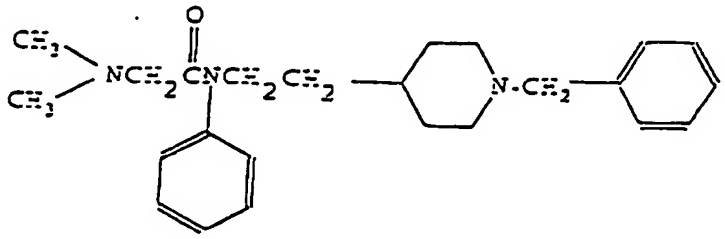
and E is a carbon or nitrogen atom;

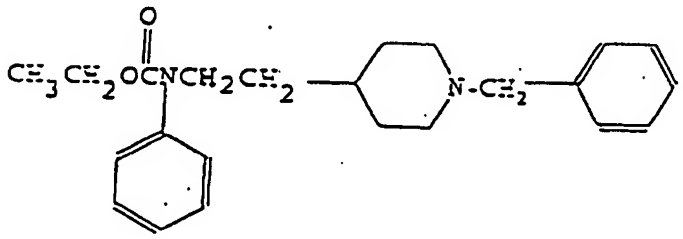
the bridging group -B- is $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 being a C_{1-6} alkyl, an acyl, a C_{1-6} alkylsulfonyl, phenyl or benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r being zero or an integer of 1 to 6 with the proviso that if B is $-NR^4-(CH_2)_r-$ then r is not zero, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ or $-CH=CH-CO-NH-(CH_2)_2-$; and

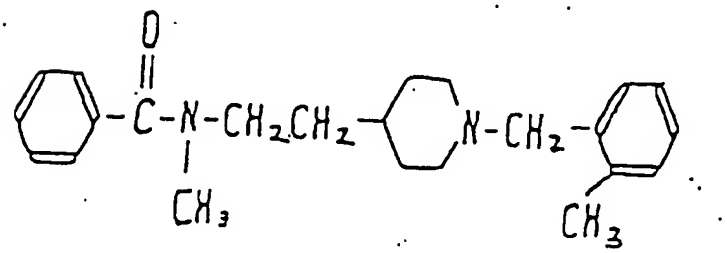
K is a phenylalkyl group in which the phenyl is optionally substituted by a C_{1-6} alkyl group which may optionally be halogenated, a C_{1-6} alkoxy group, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, a C_{1-6} alkoxycarbonyl group, an amino group, a C_{1-6} monoalkylamino group, a C_{1-6} dialkylamino group, a carbamoyl group, a C_{1-6} acylamino group, a cyclohexyloxycarbonyl group, a C_{1-6} alkylaminocarbonyl group, a C_{1-6} alkylcarbonyloxy group, a hydroxyl group, a formyl group or a C_{1-6} alkoxy-C_{1-6} alkyl group.

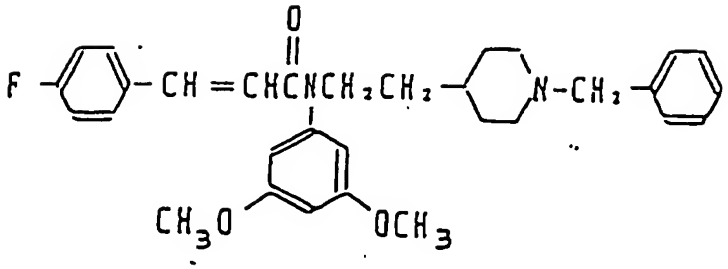
14. A process for preparing a pharmaceutical composition comprising the step of mixing a pharmaceutically acceptable carrier and a cyclic amine compound or a pharmaceutically acceptable salt thereof of any one of the formula

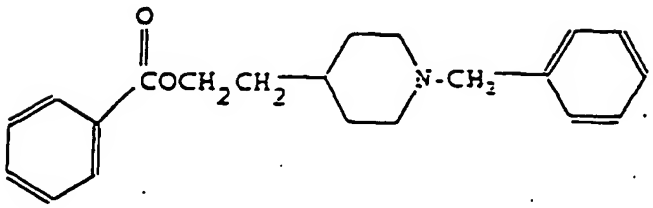


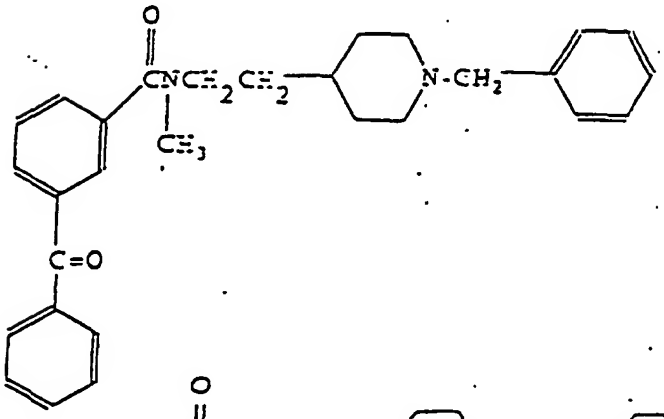


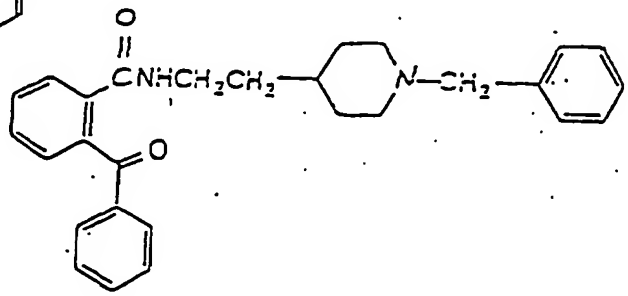


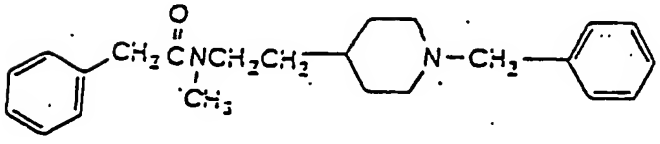


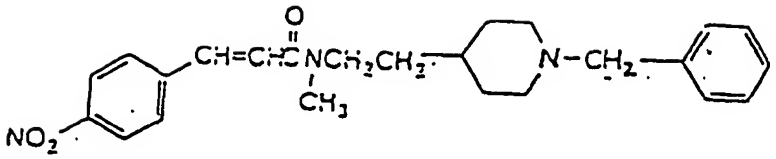


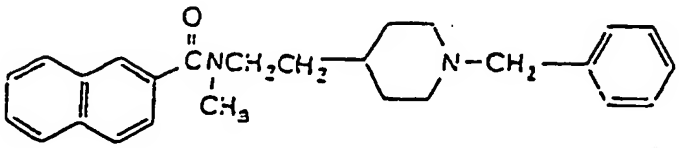




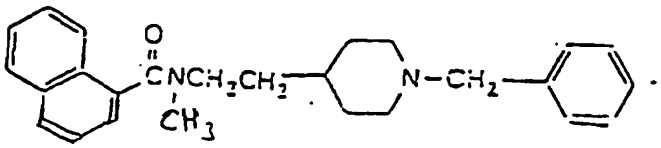








and



15. A process for preparing a pharmaceutical composition comprising the step of mixing a pharmaceutically acceptable carrier and a cyclic amine compound or a pharmaceutically acceptable salt thereof which is
4-(N-Benzylpiperidin-4-yl)-(4-methoxy) butyrophenone.

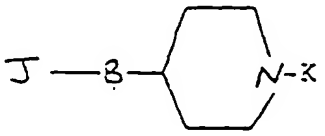
16. A process for preparing a pharmaceutical composition comprising the step of mixing a pharmaceutically acceptable carrier and a cyclic amine compound or a pharmaceutically acceptable salt thereof which is

Isopropyl 3-(N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-{2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-quinoxalinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-2-quinoxalinecarboxamide,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl] -4-fluorocinnamide,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamide,
N-Methyl-N-[2-(1-adamanthanemethylpiperidin-4-yl)ethyl] benzamide,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamide,
4- (1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanone,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamide,
Ethyl 3-(N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorobenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazinecarboxamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamide,
N-[2-(1-Furfrylpiperidin-4-yl)ethyl]benzamide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilide,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl nicotinamide or 4-(1-Benzylpiperidin-4-yl)propionanilide.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, LI, DE, FR, GB, IT, LU, NL, SE

1. Cyclische Amin-Verbindung mit der folgenden Formel (XXV) oder ein pharmazeutisch annehmbares Salz davon:

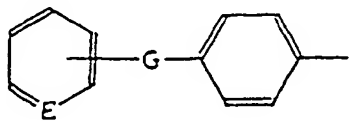


(XXV)

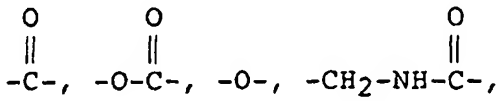
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

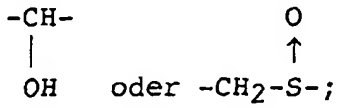
(ii)



worin G darstellt:



$-CH_2-O-$, $-CH_2-SO_2-$,

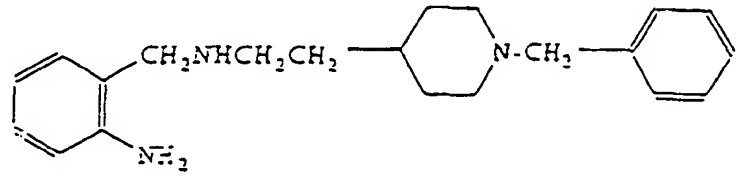


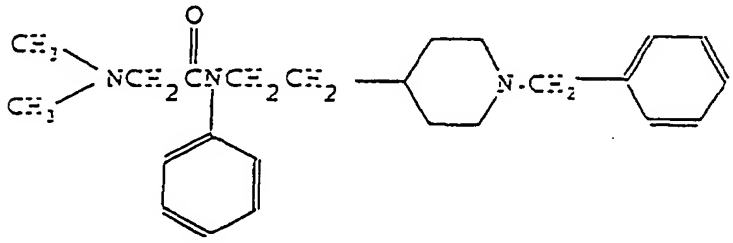
und E ist ein Kohlenstoff- oder Stickstoffatom;

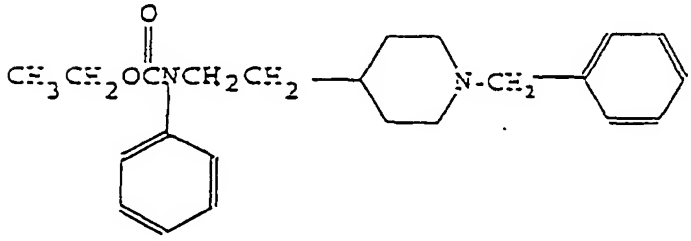
Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 unter der Voraussetzung, daß wenn B $-NR^4-(CH_2)_r-$ ist, r nicht Null, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ oder $-CH=CH-CO-NH-(CH_2)_2-$ ist; und
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom,

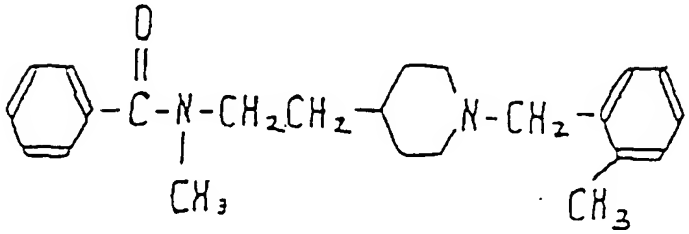
einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe.

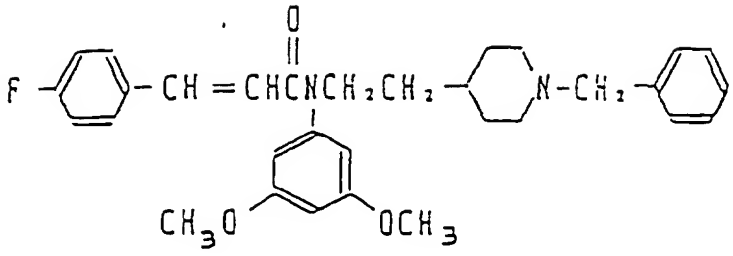
2. Cyclische Amin-Verbindung gemäß einer der Formeln:

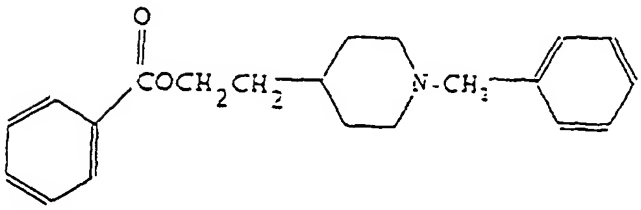


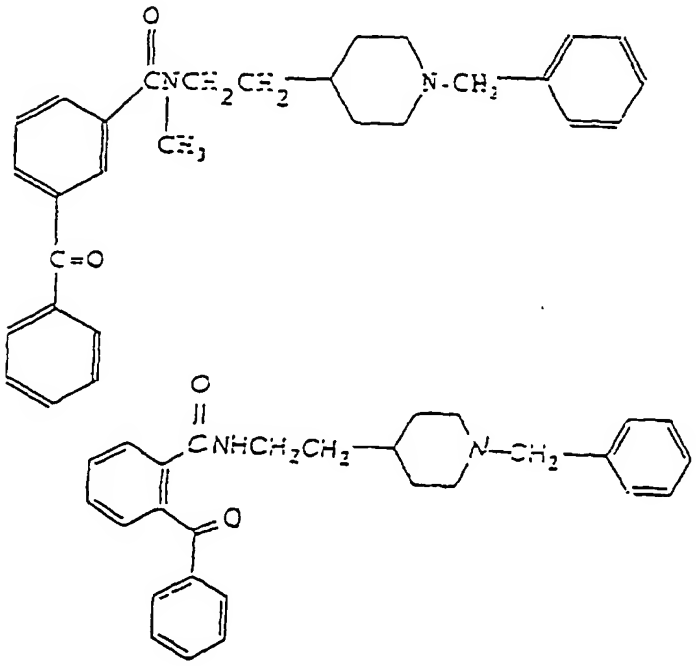


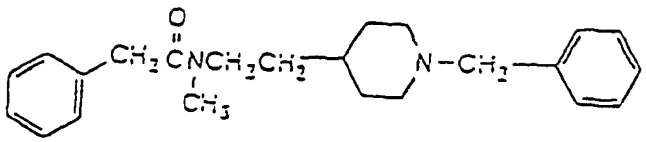


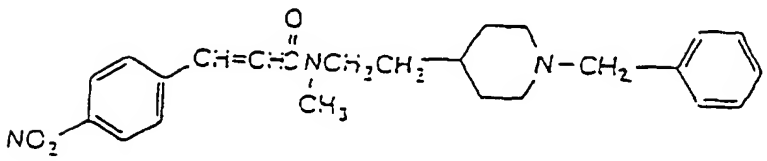


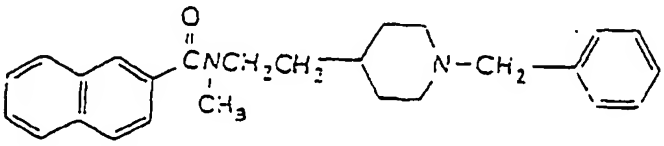




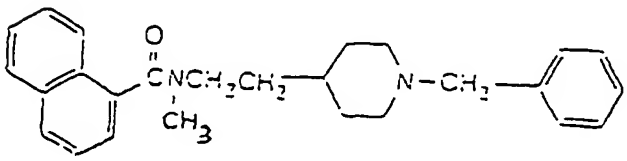








und



3. Cyclische Amin-Verbindung oder ein pharmazeutisch annehmbares Salz davon gemäß Anspruch 1, das: 4-(N-Benzylpiperidin-4-yl)-(4-methoxy)butyrophenon ist.

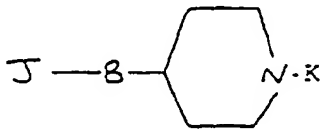
4. Cyclische Amin-Verbindung oder ein pharmazeutisch annehmbares Salz davon, das ist:

Isopropyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazincarboxylat,
N-2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-chinoxalincarboxamid,
N-2-(1-Benzylpiperidin-4-yl)ethyl]-2-chinoxalincarboxamid,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorcinnamid,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamid,
N-Methyl-N-[2-(1-adamanthanmethylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamid,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanon,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamid,
Ethyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamid}-2-pyrazincarboxylat,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorbenzamit,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazincarboxamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamid,
N-[2-(1-Furfurylpiperidin-4-yl)ethyl]benzamid,

N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylnicotinamid oder
4-(1-Benzylpiperidin-4-yl)propionanilid.

5. Therapeutische Zusammensetzung die eine pharmazeutische wirksame Menge einer cyclischen Amin-Verbindung gemäß einem der vorherigen Ansprüche oder ein pharmazeutisch annehmbares Salz davon und einen pharmazeutisch annehmbaren Träger umfaßt.

6. Verwendung einer cyclischen Amin-Verbindung gemäß Anspruch 2, 3, 4 oder mit der folgenden Formel (XXV)' oder ein pharmazeutisch annehmbares Salz davon:

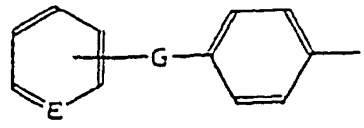


(XXV)'

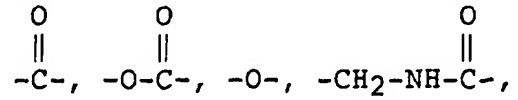
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

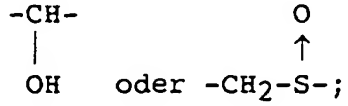
(ii)



worin G darstellt:



$-CH_2-O-$, $-CH_2-SO_2-$,



und E ist ein Kohlenstoff- oder Stickstoffatom;

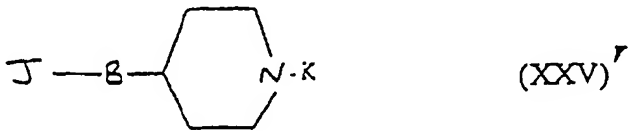
Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, -CH

(CH_3)-CO-NH-CH_2- oder -CH=CH-CO-NH-$(CH_2)_2$- ist; und
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe,
oder ein pharmazeutisch annehmbares Salz davon, zur Herstellung eines Medikaments zur Behandlung einer Erkrankung aufgrund einer Acetylcholinesterase-Aktivität.

7. Verwendung gemäß Anspruch 6, wobei das Medikament wirksam gegen Altersdemens ist.

8. Verwendung gemäß Anspruch 6, wobei das Medikament wirksam gegen Altersdemens vom Alzheimer-Typ ist.

9. Verfahren zur Herstellung eines Medikaments zur Behandlung einer Erkrankung aufgrund einer Acetylcholinesterase-Aktivität, **gekennzeichnet durch** die Verwendung als ein essentieller Bestandteil dieses Mittels einer cyclischen Amin-Verbindung gemäß Ansprüchen 2, 3, 4 oder mit der folgenden Formel (XXV)' oder einem pharmakologisch annehmbaren Salz davon:

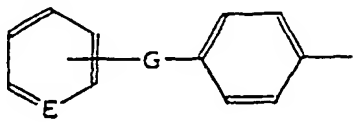


(XXV)'

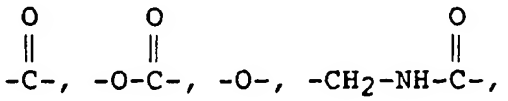
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

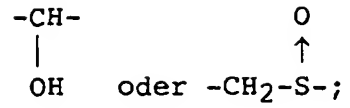
(ii)



worin G darstellt:



$-CH_2-O-$, $-CH_2-SO_2-$,

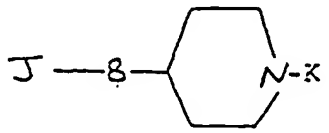


und E ist ein Kohlenstoff- oder Stickstoffatom;

Die Verbindungsgruppe B ist -CO-$(CH_2)_r$-, NR^4-$(CH_2)_r$-, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, -CH=CH-$(CH_2)_r$-, -OCOO-$(CH_2)_r$-, -OOC-NH-$(CH_2)_r$-, $-CH_2$-CO-NH-$(CH_2)_r$-, -$(CH_2)_2$-CO-NH-$(CH_2)_r$-, -CH(OH)-$(CH_2)_r$-, r ist Null oder eine ganze Zahl von 1 bis 6 -CO-CH=CH-CH_2-, -CO-CH_2-CH(OH)-CH_2-, -CH (CH_3)-CO-NH-CH_2- oder -CH=CH-CO-NH-$(CH_2)_2$- ist; und
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe.

Patentansprüche für folgende Vertragsstaaten : ES, GR

1. Cyclische Amin-Verbindung mit der folgenden Formel (XXV) oder ein pharmazeutisch annehmbares Salz davon:

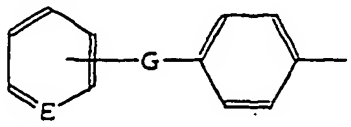


(XXV)

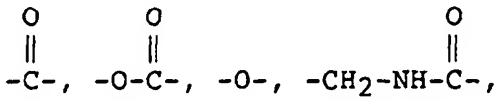
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

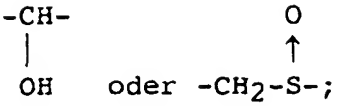
(ii)



worin G darstellt:



$-CH_2-O-$, $-CH_2-SO_2-$,

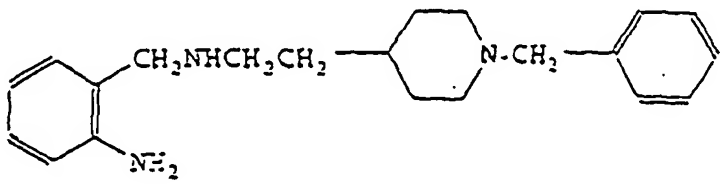


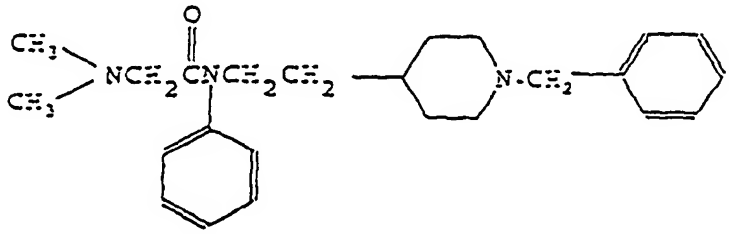
und E ist ein Kohlenstoff- oder Stickstoffatom;

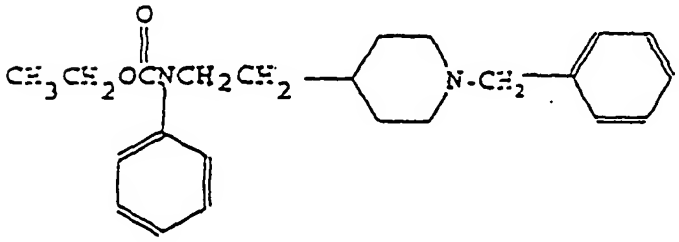
Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOO-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 unter der Voraussetzung, daß wenn B $-NR^4-(CH_2)_r-$ ist, r nicht Null, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ oder $-CH=CH-CO-NH-(CH_2)_2-$ ist; und

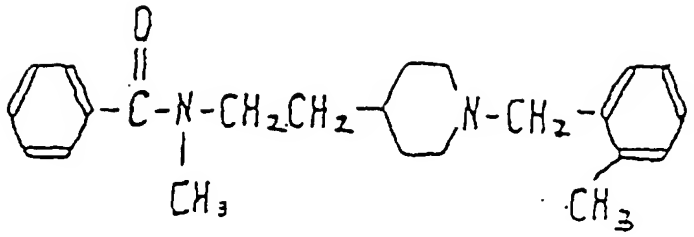
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe.

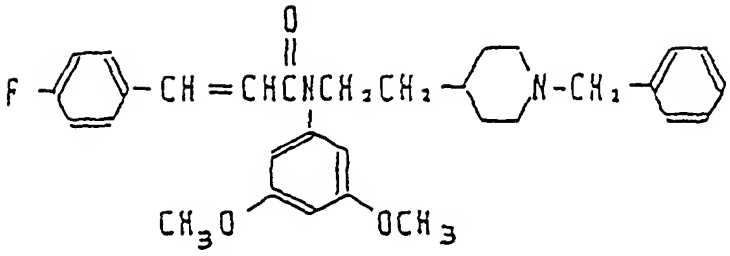
2. Cyclische Amin-Verbindung gemäß einer der Formeln:

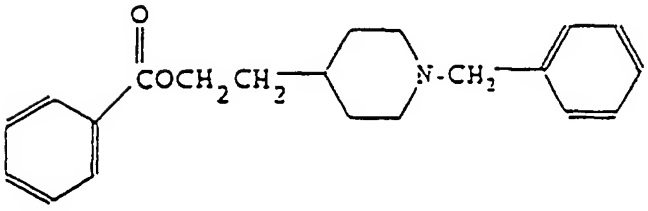


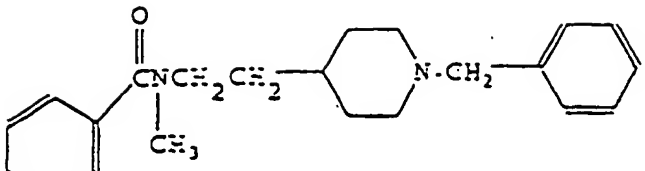


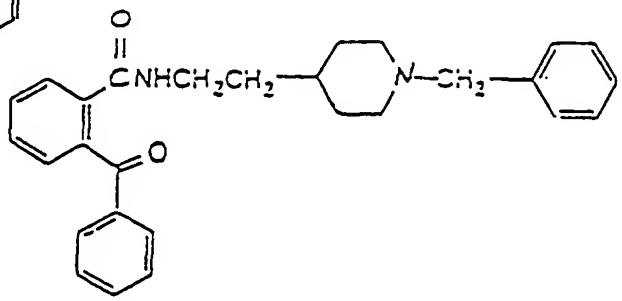


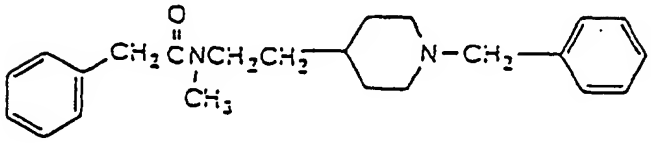


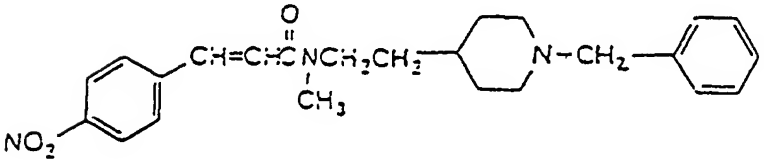


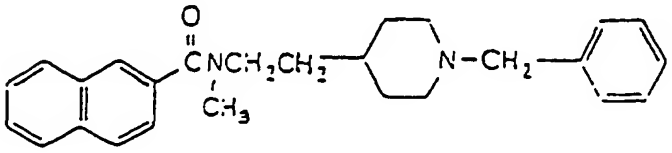




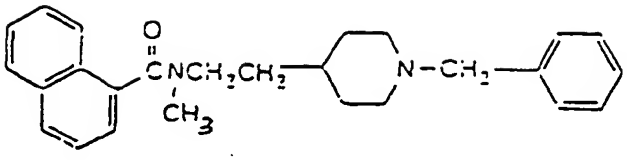








und



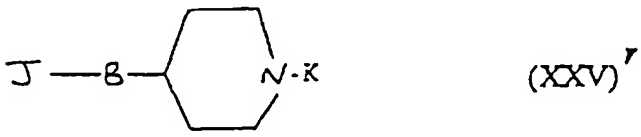
3. Cyclische Amin-Verbindung oder ein pharmazeutisch annehmbares Salz davon gemäß Anspruch 1, das: 4-(N-Benzylpiperidin-4-yl)-(4-methoxy)butyrophenon ist.

4. Cyclische Amin-Verbindung oder ein pharmazeutisch annehmbares Salz davon, das ist:

Isopropyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazincarboxylat,
N-2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-chinoxalincarboxamid,
N-2-(1-Benzylpiperidin-4-yl)ethyl]-2-chinoxalincarboxamid,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorcinnamid,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamid,
N-Methyl-N-[2-(1-adamanthanmethylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamid,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanon,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamid,
Ethyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamid}-2-pyrazincarboxylat,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazincarboxamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamid,
N-[2-(1-Furfurylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylnicotinamid oder
4-(1-Benzylpiperidin-4-yl)propionanilid.

5. Therapeutische Zusammensetzung die eine pharmazeutische wirksame Menge einer cyclischen Amin-Verbindung gemäß einem der vorherigen Ansprüche oder ein pharmazeutisch annehmbares Salz davon und einen pharmazeutisch annehmbaren Träger umfaßt.

6. Verwendung einer cyclischen Amin-Verbindung mit der folgenden Formel (XXV)' oder ein pharmazeutisch annehmbares Salz davon:

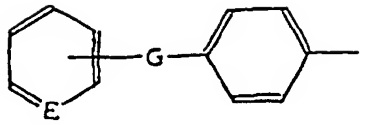


(XXV)'

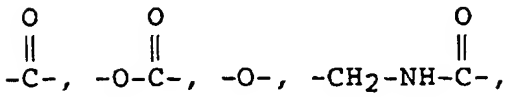
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

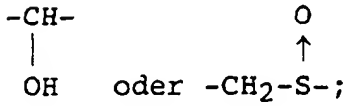
(ii)



worin G darstellt:



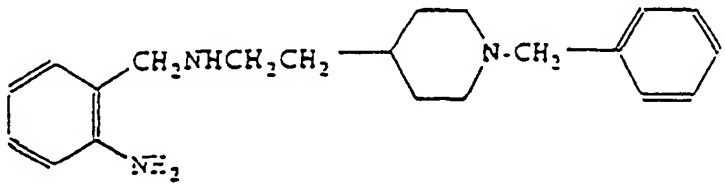
$-CH_2-O-$, $-CH_2-SO_2-$,

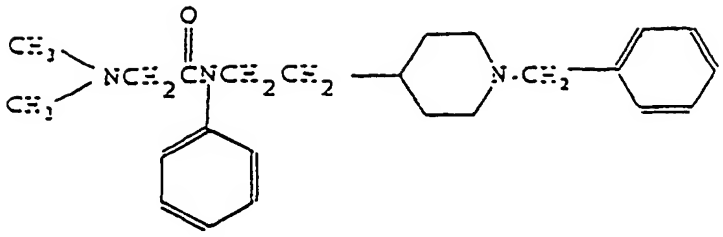


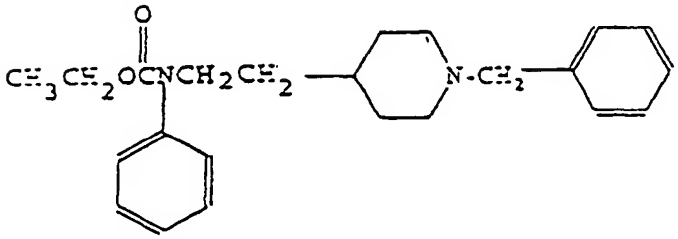
und E ist ein Kohlenstoff- oder Stickstoffatom;

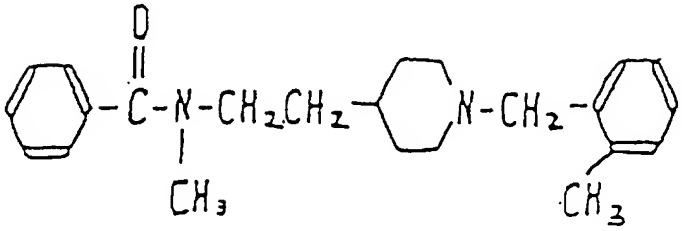
Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ oder $-CH=CH-CO-NH-(CH_2)_2-$ ist; und
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe,
oder ein pharmazeutisch annehmbares Salz davon, zur Herstellung eines Medikaments zur Behandlung einer Erkrankung aufgrund einer Acetylcholinesterase-Aktivität.

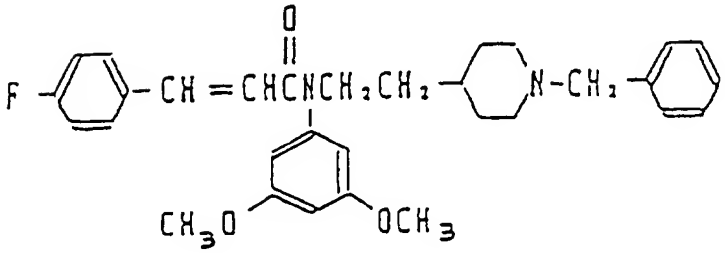
7. Verwendung einer cyclischen Amin-Verbindung oder eines pharmazeutischen annehmbaren Salzes davon gemäß einer der Formeln:

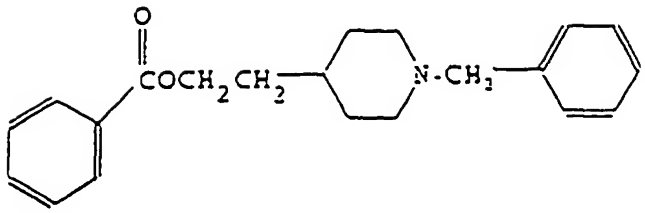


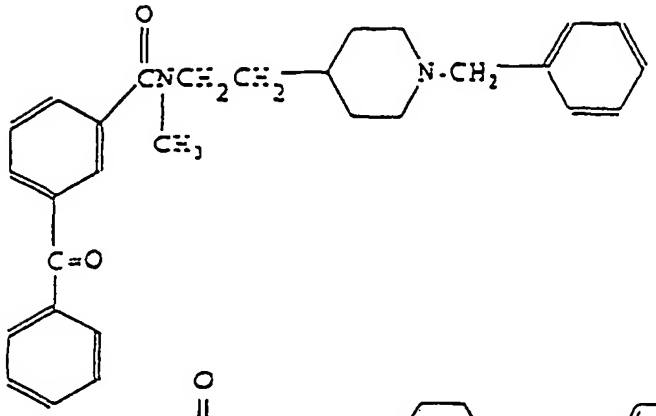


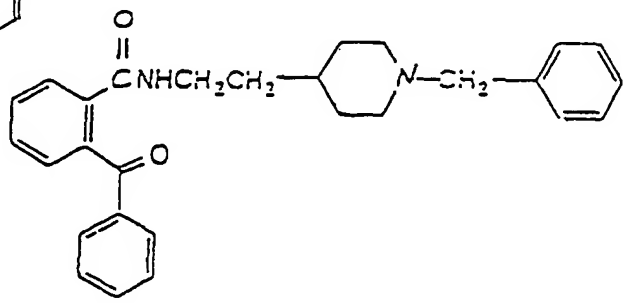


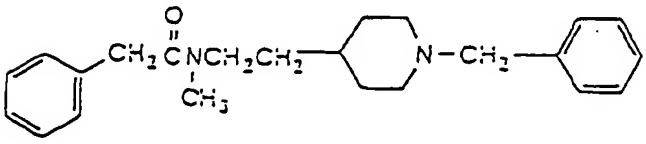


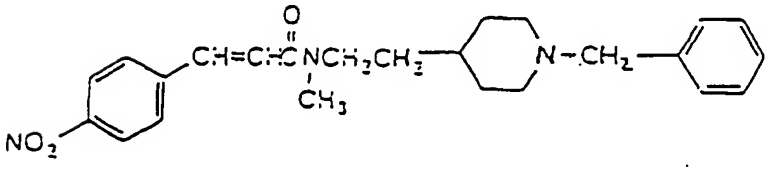


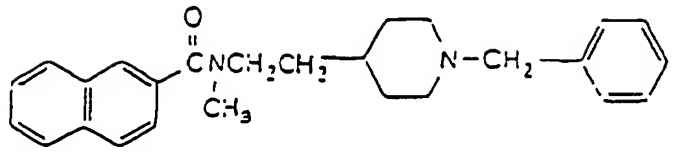




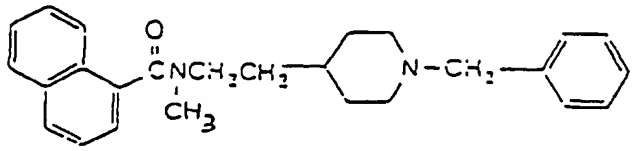








und



Zur Herstellung eines Medikaments zur Behandlung einer Erkrankung aufgrund einer Acetylcholinesterase-Aktivität.

8. Verwendung gemäß an 6, wobei die cyclische Amin-Verbindung 4-(N-Benzylpiperidin-4-yl)-(4-methoxy)butyrophenon ist.

9. Verwendung einer cyclischen Amin-Verbindung oder eines pharmazeutisch annehmbaren Salzes davon, welches ist:

Isopropyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazincarboxylat,
N-2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-chinoxalincarboxamid,
N-2-(1-Benzylpiperidin-4-yl)ethyl]-2-chinoxalincarboxamid,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorcinnamid,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamid,
N-Methyl-N-[2-(1-adamanthanmethylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamid,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanon,
N-(4-Pyridyl)-3-(l-benzylpiperidin-4-yl)propionamid,
Ethyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamid}-2-pyrazincarboxylat,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazincarboxamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamid,
N-[2-(1-Furfurylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylnicotinamid oder
4-(1-Benzylpiperidin-4-yl)propionanilid

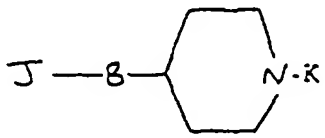
zur Herstellung eines Medikaments zur Behandlung eienr Erkrankung aufgrund einer Acetylcholinesterase-Aktivität.

10. Verwendung gemäß einem der Ansprüche Anspruch 6 bis 9, wobei das Medikament wirksam gegen Altersdemens ist.

11. Verwendung gemäß einem der Ansprüche 6 bis 9, wobei das Medikament wirksam gegen Altersdemens vom Alzheimer-Typ ist.

12. Verfahren zur Herstellung eines Medikaments zur Behandlung einer Erkrankung aufgrund einer Acetylcholine-

sterase-Aktivität, **gekennzeichnet durch** die Verwendung als ein essentieller Bestandteil dieses Mittels einer cyclischen Amin-Verbindung gemäß Ansprüchen 7, 8, 9 oder mit der folgenden Formel (XXV)' oder einem pharmakologisch annehmbaren Salz davon:

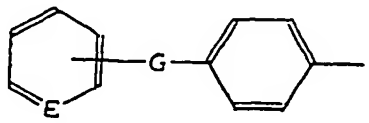


(XXV)'

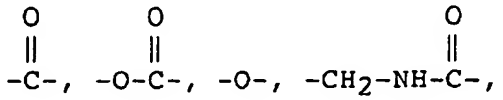
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

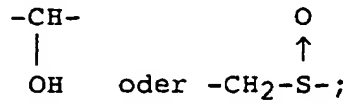
(ii)



worin G darstellt:



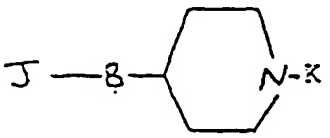
$-CH_2-O-$, $-CH_2-SO_2-$,



und E ist ein Kohlenstoff- oder Stickstoffatom;

Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ oder $-CH=CH-CO-NH-(CH_2)_2-$ ist; und
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe.

13. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung umfassend den Schritt des Mischens eines pharmazeutisch annehmbares Trägers und einer cyclischen Amin-Verbindung mit der folgenden Formel (XXV) oder eines pharmazeutisch annehmbaren Salzes davon:

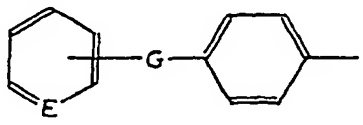


(XXV)

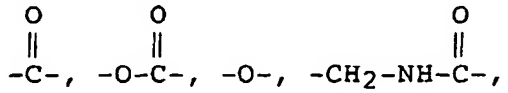
worin J ist:

(i) eine Phenyl-Gruppe, gegebenenfalls substituiert mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonyloxy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-Alkyl-Gruppe oder

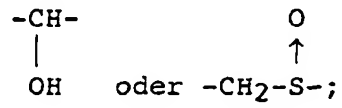
(ii)



worin G darstellt:



$-CH_2-O-$, $-CH_2-SO_2-$,



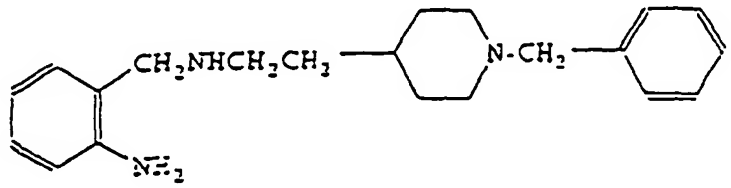
und E ist ein Kohlenstoff- oder Stickstoffatom;

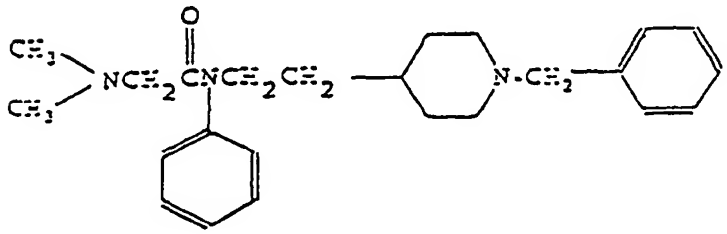
Die Verbindungsgruppe B ist $-CO-(CH_2)_r-$, $NR^4-(CH_2)_r-$, R^4 ist ein C_{1-6}-Alkyl, ein Acyl, ein C_{1-6}-Alkylsulfonyl, Phenyl oder Benzyl, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, $-OOC-NH-(CH_2)_r-$, $-CH_2-CO-NH-(CH_2)_r-$, $-(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r ist Null oder eine ganze Zahl von 1 bis 6 unter der Voraussetzung, daß wenn B $-NR^4-(CH_2)_r-$ ist, r nicht Null, $-CO-CH=CH-CH_2-$, $-CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-CO-NH-CH_2-$ oder $-CH=CH-CO-NH-(CH_2)_2-$ ist; und

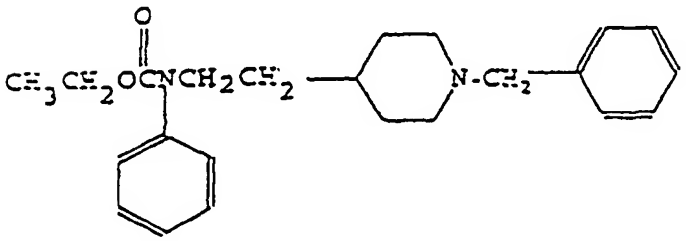
K ist eine Phenylalkyl-Gruppe, bei der das Phenyl gegebenenfalls substituiert sein kann mit einer C_{1-6}-Alkyl-Gruppe, die gegebenenfalls halogeniert sein kann, einer C_{1-6}-Alkoxy-Gruppe, einer Nitro-Gruppe, einem Halogenatom, einer Carboxyl-Gruppe, einer Benzyloxy-Gruppe, einer C_{1-6}-Alkoxycarbonyl-Gruppe, einer Amino-Gruppe, einer C_{1-6}-Monoalkylamino-Gruppe, einer C_{1-6}-Dialkylamino-Gruppe, einer Carbamoyl-Gruppe, einer C_{1-6}-Acylamino-Gruppe, einer Cyclohexyloxycarbonyl-Gruppe, einer C_{1-6}-Alkylaminocarbonyl-Gruppe, einer C_{1-6}-Alkylcarbonylo-

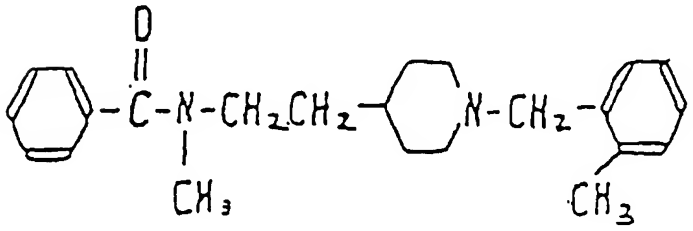
xy-Gruppe, einer Hydroxyl-Gruppe, einer Formyl-Gruppe oder einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe.

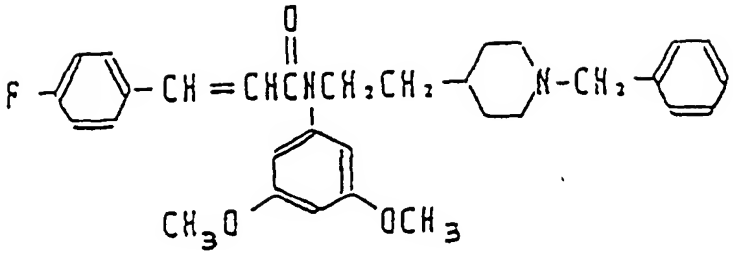
14. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung umfassend den Schritt des Mischens eines pharmazeutisch annehmbaren Trägers und einer cyclischen Amin-Verbindung oder eines pharmazeutisch annehmbaren Salzes davon gemäß einer der folgenden Formeln:

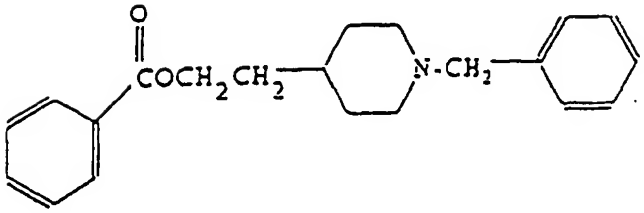


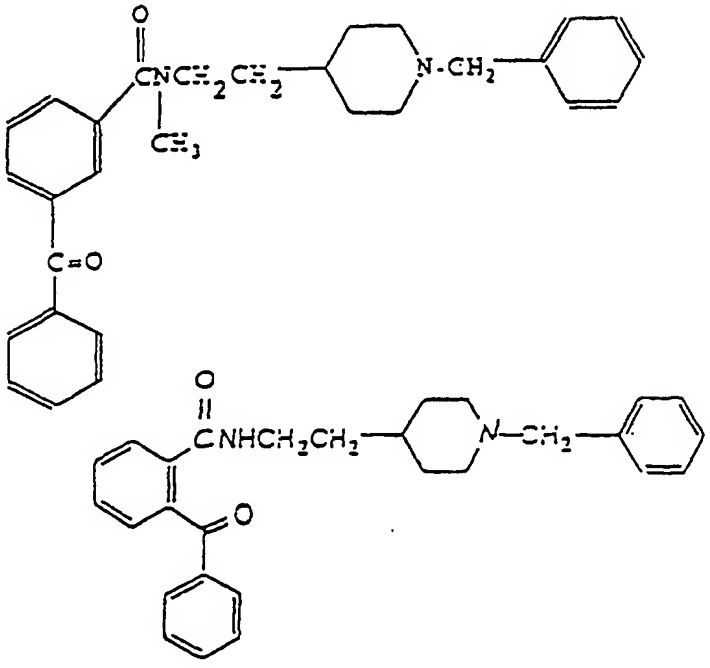


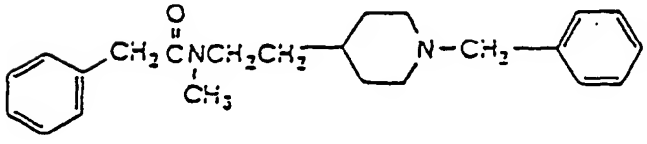


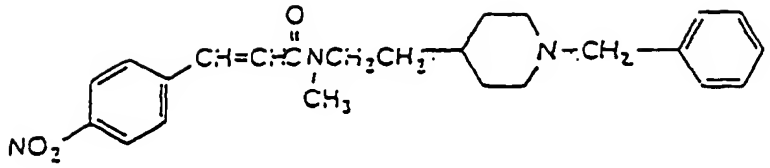


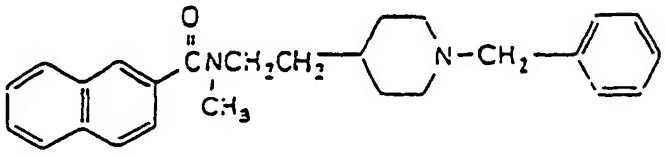




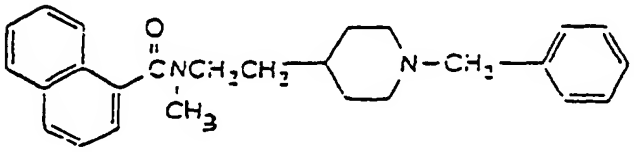








und



15. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung umfassend den Schritt des Mischens eines pharmazeutisch annehmbaren Trägers und einer cyclischen Amin-Verbindung oder eines pharmazeutisch annehmbaren Salzes davon, das 4-(N-Benzylpiperidin-4-yl)-4-methoxy)butyrophenon ist.

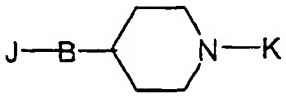
16. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung umfassend den Schritt des Mischens eines pharmazeutisch annehmbaren Trägers und einer cyclischen Amin-Verbindung oder eines pharmazeutisch annehmbaren Salzes davon, welches ist:

Isopropyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamido}-2-pyrazincarboxylat,
N-2-[1-(4-Hydroxybenzyl)piperidin-4-yl]ethyl}-2-chinoxalincarboxamid,
N-2-(1-Benzylpiperidin-4-yl)ethyl]-2-chinoxalincarboxamid,
N-(3,5-Dimethoxyphenyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-4-fluorcinnamid,
N-[(1-Benzylpyrrolidin-3-yl)methyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-3-furancarboxamid,
N-Methyl-N-[2-(1-adamanthanmethylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Cyclohexylmethylpiperidin-4-yl)ethyl]-N-methylbenzamid,
4-(1-Benzylpiperidin-4-yl)-1-(4-pyridyl)butanon,
N-(4-Pyridyl)-3-(1-benzylpiperidin-4-yl)propionamid,
Ethyl-3-{N-[2-(1-benzylpiperidin-4-yl)ethyl]carboxamid}-2-pyrazincarboxylat,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenyl-4-fluorbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylbenzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylpyrazincarboxamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-(4-pyridyl)acetamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-methylfurancarboxamid,
N-[2-(1-Furfurylpiperidin-4-yl)ethyl]benzamid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]acetanilid,
N-[2-(1-Benzylpiperidin-4-yl)ethyl]-N-phenylnicotinamid oder
4-(1-Benzylpiperidin-4-yl)propionanilid.

Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, LI, DE, FR, GB, IT, LU, NL, SE

1. Composé amine cyclique répondant à la formule suivante (XXV) ou un sel pharmacologiquement acceptable de celui-ci :

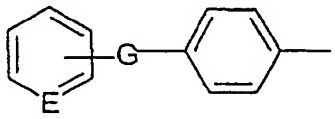


(XXV)

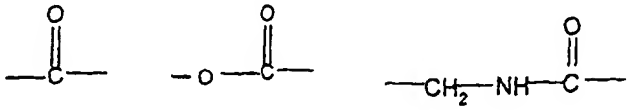
dans laquelle

J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



Dans laquelle G représente



-O-, $-CH_2-O$, $-CH_2-SO_2-$,

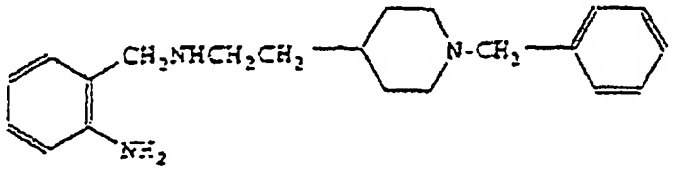
ou ;

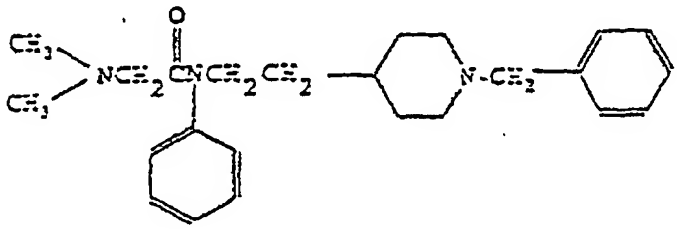
et E est un atome de carbone ou d'azote ;
le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6}

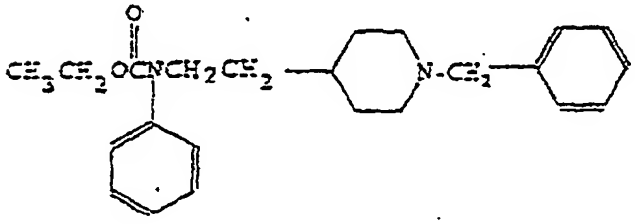
sulfonyle, phényle ou benzyle, -CH=CH-$(CH_2)_r$-, -OCOO-$(CH_2)_r$-, -OOC-NH-$(CH_2)_r$-, (CH_2) -CO-NH-$(CH_2)_r$-, $(CH_2)_2$-CO-NH-$(CH_2)_r$-, -CH(OH)-$(CH_2)_r$-, r étant zéro ou un entier de 1 à 6 à la condition que si B est -NR^4-$(CH_2)_r$-, alors r n'est pas zéro, CO-CH=CH-CH_2, CO- CH_2-CH(OH)-CH_2-, -$CH(CH_3)$-Co-NH-CH_2- ou -CH=CH-CO-NH-$(CH_2)_2$- ; et

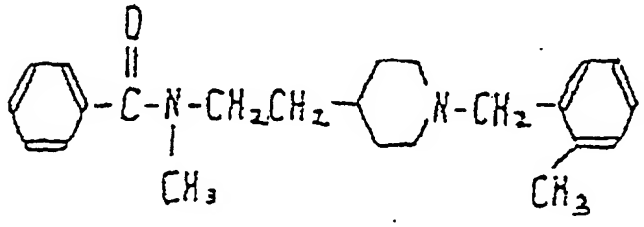
K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}.

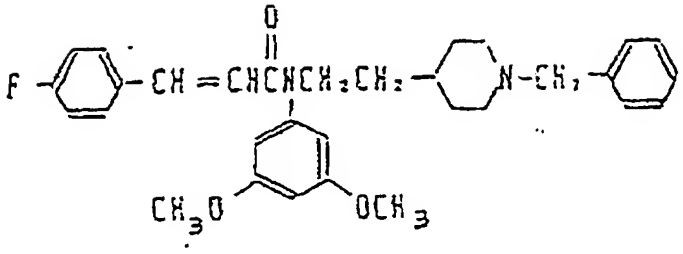
2. Composé amine cyclique de l'une quelconque des formules :

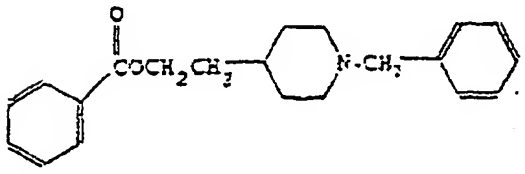


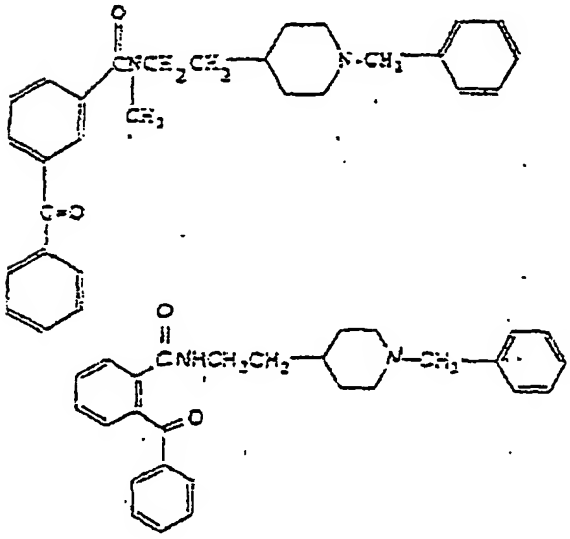


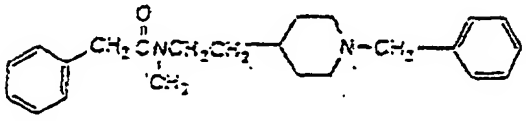


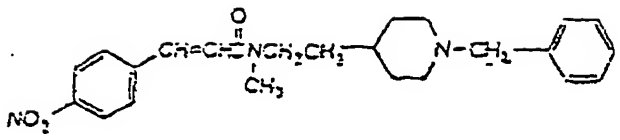


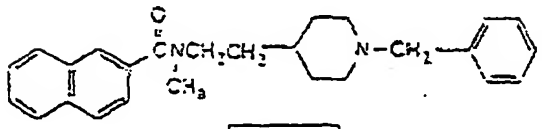












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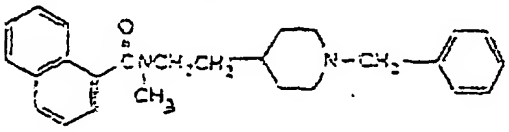


3. Composé amine cyclique ou sel acceptable sur le plan pharmacologique de celui-ci selon la revendication 1, qui est la :

   4-(N-benzylpipéridin-4-yl)-(4-méthoxy)butyrophénone.

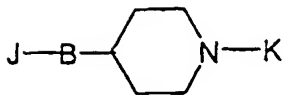
4. Composé amine cyclique ou sel acceptable sur le plan pharmacologique de celui-ci, qui est :

   Isopropyl 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
   N-{2-[1-(4-hydroxybenzyl)pipéridin-4-yl]éthyl}-2-quinoxaline carboxamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-2-quinoxaline carboxamide,
   N-(3,5-diméthoxyphényl)-N-[2-(1-benzylpipéridine-4-yl)éthyl]-4-fluorocinnamide,
   N-[(1-benzylpyrrolidin-3-yl)méthyl]-benzamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-3-furancarboxamide,
   N-méthyl-N-[2-(1-adamanthanemethylpipéridin-4-yl)éthyl]-benzamide,
   N-[2-(1-cyclohexylméthylpipéridin-4-yl)éthyl]-N-méthylbenzamide,
   4-(1-benzylpipéridin-4-yl)-1-(4-pyrridyl)butanone,
   N-(4-pyrridyl)-3-(1-benzylpipéridin-4-yl)-proprionamide,
   Ethyle 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
   N-[2-1(1-benzylpipéridin-4-yl)éthyl]-N-phényl-4-fluorobenzamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylbenzamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylpyrazinecarboxamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-(4-pyridyl)acétamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-méthylfurancarboxamide,
   N-[2-(1-furfrylpipéridin-4-yl)éthyl]benzamide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]acétanilide,
   N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylnicotamide ou
   4-(1-benzylpipéridin-4-yl)proprionanilide.

5. Composition thérapeutique comprenant une quantité efficace sur le plan pharmacologique d'un composé amine cyclique comme défini dans l'une quelconque des revendications précédentes ou un sel pharmacologiquement acceptable de celui-ci et un véhicule pharmacologiquement acceptable.

6. Utilisation du composé amine cyclique comme défini dans la revendication 2, 3, 4 ou répondant à la formule suivante (XXV)'

   Ou un sel pharmacologiquement acceptable de celui-ci :

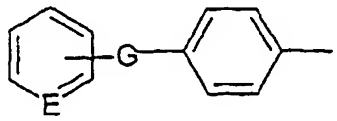


(XXV)'

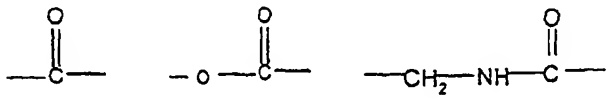
dans laquelle

J est :

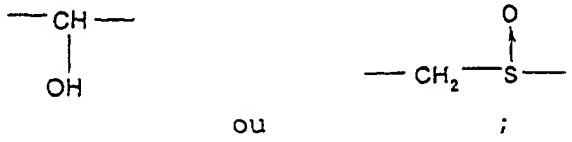
(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



dans laquelle G représente



$-O-$,$-CH_2-O$, $-CH_2-SO_2-$,



et E est un atome de carbone ou d'azote ;

le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6 $CO-CH=CH-CH_2$, $CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-Co-NH-CH_2-$ ou $-CH=CH-CO-NH-(CH_2)_2$; et

K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbony-

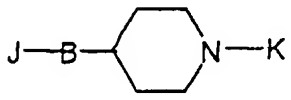
loxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6},

ou un sel pharmacologiquement acceptable de celui-ci,
pour la préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase.

7. Utilisation comme revendiqué dans la revendication 6, dans laquelle le médicament est efficace contre la démence sénile.

8. Utilisation comme revendiqué dans la revendication 6, dans laquelle le médicament est efficace contre la démence sénile de type Alzheimer.

9. Procédé de préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase, caractérisé dans l'utilisation, à titre de constituant essentiel dudit agent, d'un composé amine cyclique comme défini dans les revendications 2, 3, 4 ou répondant à la formule suivante (XXV)', ou un sel pharmacologiquement acceptable de celui-ci :

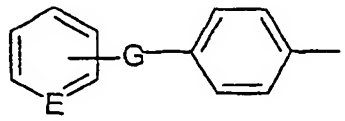


(XXV)'

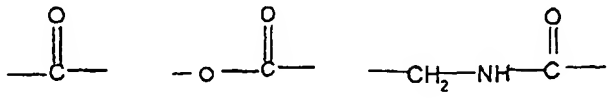
dans laquelle

J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



dans laquelle G représente



-O-, $-CH_2-O$, $-CH_2-SO_2-$,

ou

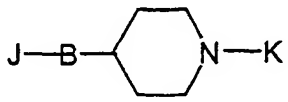
et E est un atome de carbone ou d'azote ;

le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6 $CO-CH=CH-CH_2$, $CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-Co-NH-CH_2-$ ou $-CH=CH-CO-NH-(CH_2)_2-$; et

K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}.

Revendications pour les Etats contractants suivants : ES, GR

1. Composé amine cyclique répondant à la formule suivante (XXV) ou un sel pharmacologiquement acceptable de celui-ci :

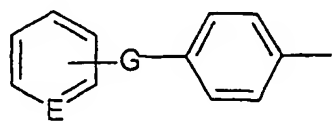


(XXV)

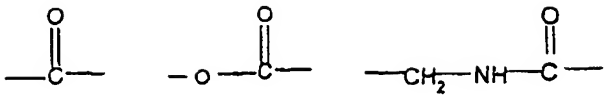
dans laquelle

J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



dans laquelle G représente



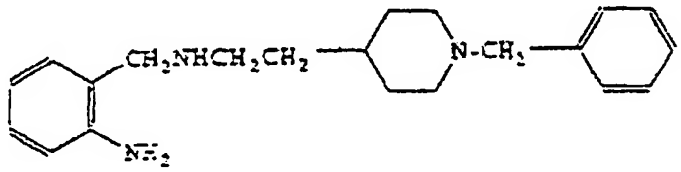
-O-, $-CH_2-O$, $-CH_2-SO_2-$,

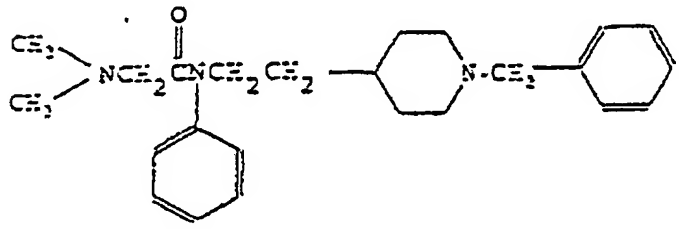
et E est un atome de carbone ou d'azote ;

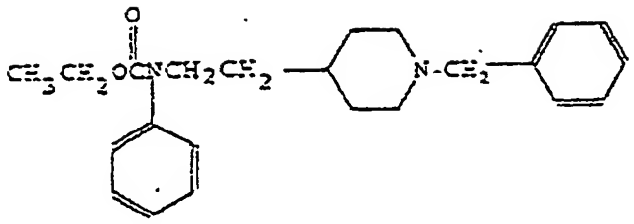
le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6 à la condition que si B est $-NR^4-(CH_2)_r-$, alors r n'est pas zéro, $CO-CH=CH-CH_2$, $CO-CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-Co-NH-CH_2-$ ou $-CH=CH-CO-NH-(CH_2)_2-$; et

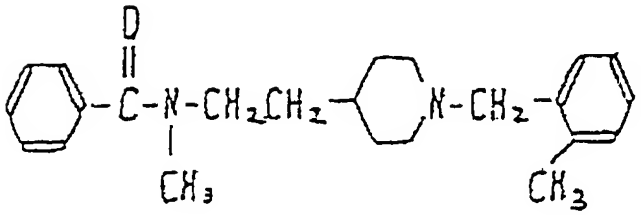
K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}.

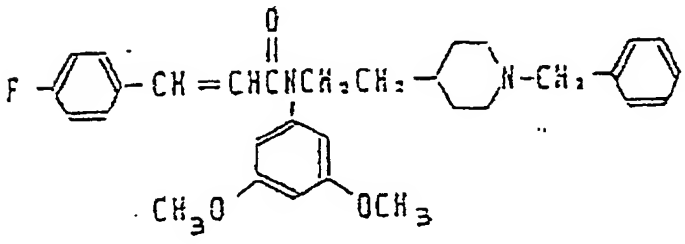
2. Composé amine cyclique de l'une quelconque des formules :

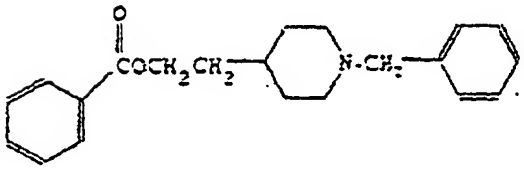


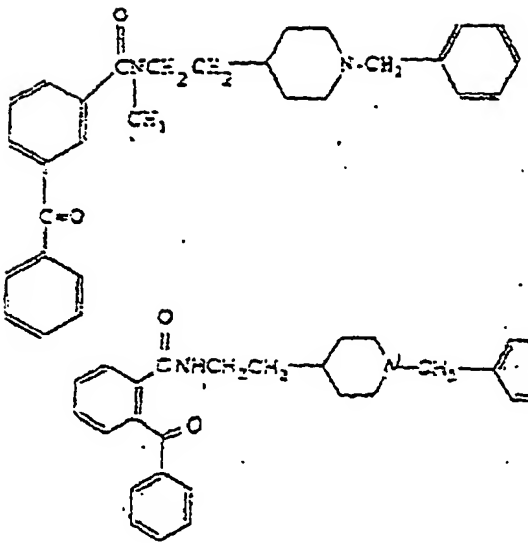


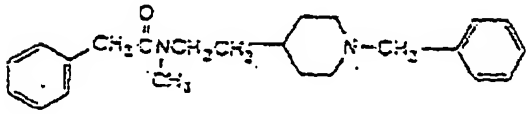


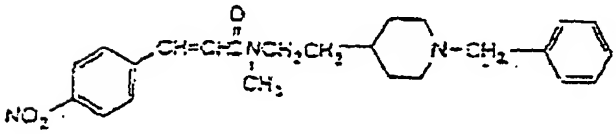


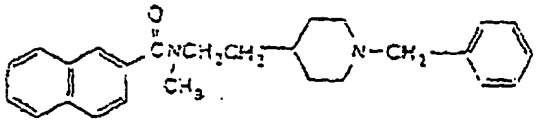




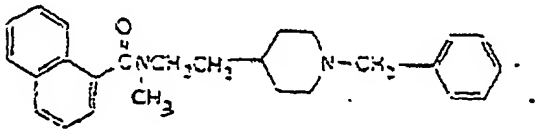








et



3. Composé amine cyclique ou sel acceptable sur le plan pharmacologique de celui-ci selon la revendication 1, qui est la :

   4-(N-benzylpipéridin-4-yl)-(4-méthoxy)butyrophénone.

4. Composé amine cyclique ou sel acceptable sur le plan pharmacologique de celui-ci, qui est :

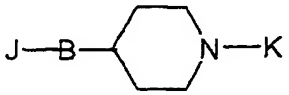
   Isopropyl 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carbcxamido}-2-pyrazinecarboxylate,

N-{2-[1-(4-hydroxybenzyl)pipéridine-4-yl]éthyl}-2-quinoxaline carboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-2-quinoxaline carboxamide,
N-(3,5-diméthoxyphényl)-N-[2-(1-benzylpipéridine-4-yl)éthyl]-4-fluorocinnamide,
N-[(1-benzylpyrrolidin-3-yl)méthyl]-benzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-3-furancarboxamide,
N-méthyl-N-[2-(1-adamanthaneméthylpipéridin-4-yl)éthyl]-benzamide,
N-[2-(1-cyclohexylméthylpipéridine-4-yl)éthyl]-N-méthylbenzamide,
4-(1-benzylpipéridine-4-yl)-1-(4-pyrridyl)butanone,
N-(4-pyrridyl)-3-(1-benzylpipéridin-4-yl)-proprionamide,
Ethyle 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-benzylpipéridin-4-yl)éthyl]-N-phényl-4-fluorobenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylbenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylpyrazinecarboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-(4-pyridyl)acétamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-méthylfurancarboxamide,
N-[2-(1-furfrylpipéridin-4-yl)éthyl]benzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]acétanilide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylnicotamide ou 4-(1-benzylpipéridin-4-yl)proprionanilide.

5. Composition thérapeutique comprenant une quantité efficace pharmacologiquement d'un composé amine cyclique comme défini dans l'une quelconque des revendications précédentes ou un sel pharmacologiquement acceptable de celui-ci et un véhicule pharmacologiquement acceptable.

6. Utilisation du composé amine cyclique comme défini dans la revendication 2, 3, 4 ou répondant à la formule suivante (XXV)'

ou un sel pharmacologiquement acceptable de celui-ci :

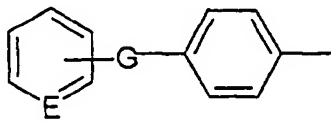


(XXV)'

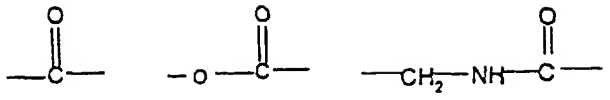
dans laquelle

J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



dans laquelle G représente



-O-, $-CH_2-O-$, $-CH_2-SO_2-$,

ou ;

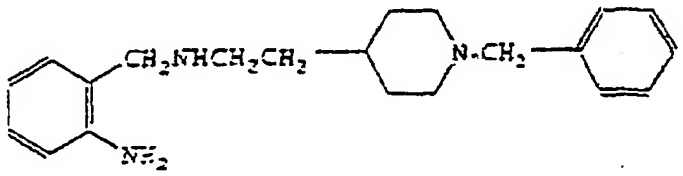
et E est un atome de carbone ou d'azote ;

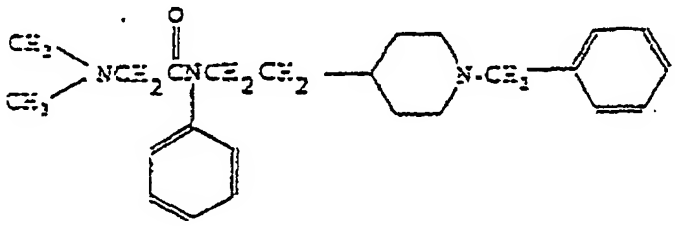
le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6 $-CO-CH=CH-CH_2$, CO- $CH_2-CH(OH)-CH_2-$, -CH $(CH_3)-Co-NH-CH_2-$ ou $-CH=CH-CO-NH-(CH_2)_2-$; et

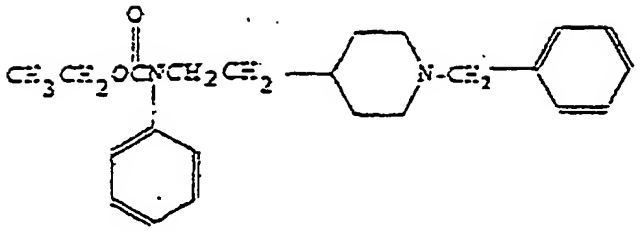
K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogène, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6},

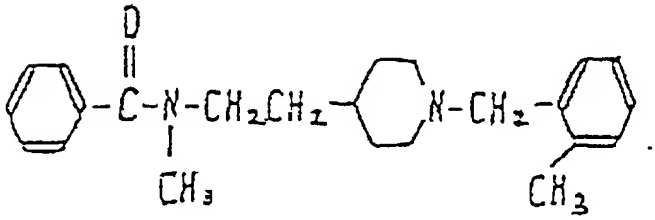
ou un sel pharmacologiquement acceptable de celui-ci,
pour la préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase.

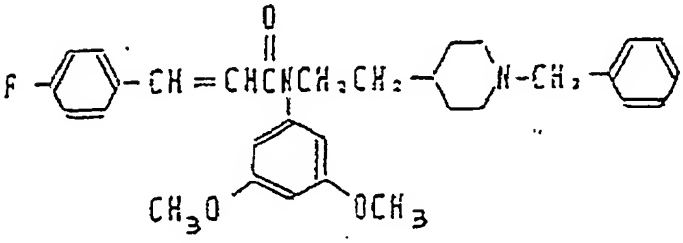
7. Utilisation d'un composé amino cyclique ou un sel pharmacologiquement acceptable de celui-ci répondant à l'une quelconque des formules :

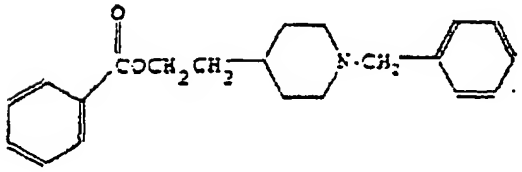


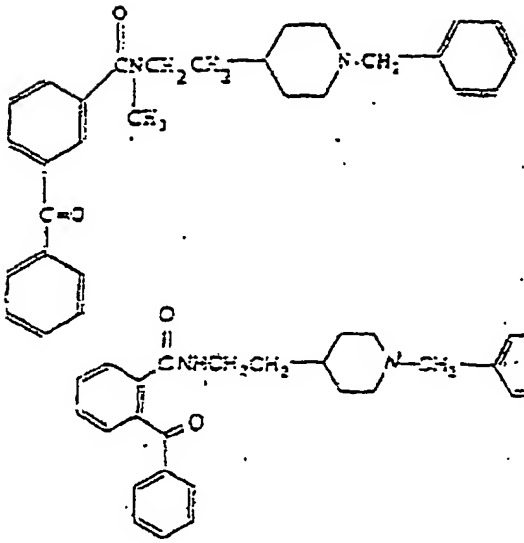


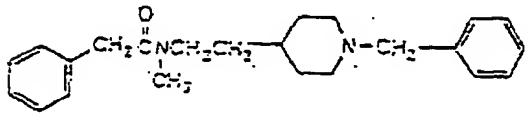


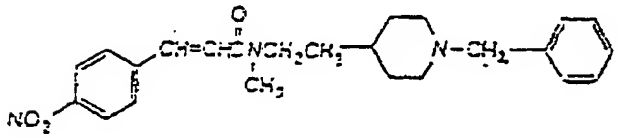


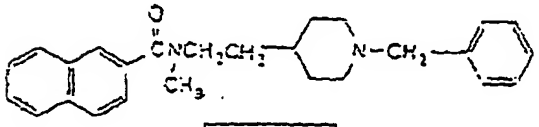












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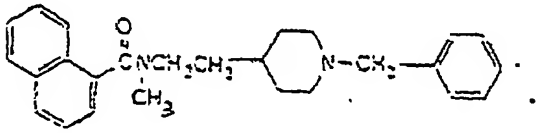


pour la préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase.

8. Utilisation selon la revendication 6, dans laquelle le composé amine cyclique est le : 4-(N-benzylpipéridin-4-yl)-(4-méthoxy)butyrophénone.

9. Utilisation d'un composé amine cyclique ou sel acceptable sur le plan pharmacologique de celui-ci, qui est :

Isopropyl 3-{N-[2-(l-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,

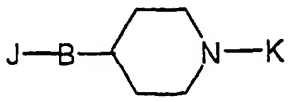
N-{2-[1-(4-hydroxybenzyl)pipéridin-4-yl]éthyl}-2-quinoxaline carboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-2-quinoxaline carboxamide,
N-(3,5-diméthoxyphényl)-N-[2-(1-benzylpipéridin-4-yl)éthyl]-4-fluorocinnamide,
N-[(1-benzylpyrrolidin-3-yl)méthyl]- benzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-3-furancarboxamide,
N-méthyl-N-[2-(1-adamanthaneméthylpipéridin-4-yl)éthyl]-benzamide,
N-[2-(1-cyclohexylméthylpipéridin-4-yl)éthyl]-N-méthylbenzamide,
4-(1-benzylpipéridin-4-yl)-1-(4-pyrridyl)butanone,
N-(4-pyrridyl)-3-(1-benzylpipéridin-4-yl)-proprionamide,
Ethyle 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-benzylpipéridin-4-yl)éthyl]-N-phényl-4-fluorobenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylbenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylpyrazinecarboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-(4-pyridyl)acétamide,
N-(2-(1-benzylpipéridin-4-yl)éthyl]-N-méthylfurancarboxamide,
N-[2-(1-furfrylpipéridin-4-yl)éthyl]benzamide,
N-[2-(1-benzylpipéridine-4-yl)éthyl]acétanilide,
N-[2-(1-benzylpipéridine-4-yl)éthyl]-N-phénylnicotamide ou 4-(1-benzylpipéridine-4-yl)proprionanilide.

pour la préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase.

10. Utilisation comme revendiqué dans l'une quelconque des revendications 6 à 9, dans laquelle le médicament est efficace contre la démence sénile.

11. Utilisation comme revendiqué dans l'une quelconque des revendications 6 à 9, dans laquelle le médicament est efficace contre la démence sénile de type Alzheimer.

12. Procédé de préparation d'un médicament pour le traitement d'une affection due à l'activité de l'acétylcholinestérase, caractérisé dans l'utilisation, à titre de constituant essentiel dudit agent, d'un composé amine cyclique comme défini dans les revendications 7, 8, 9 ou répondant à la formule suivante (XXV)', ou un sel pharmacologiquement acceptable de celui-ci :

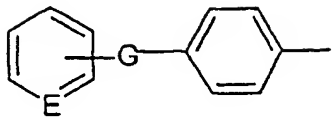


(XXV)'

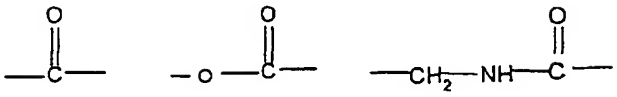
dans laquelle

J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}; ou
(ii)



dans laquelle G représente



-O-, $-CH_2-O$, $-CH_2-SO_2-$,

ou ;

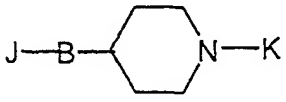
et E est un atome de carbone ou d'azote ;

le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6

$CO-CH=CH-CH_2$, CO- $CH_2-CH(OH)-CH_2-$, $-CH(CH_3)-Co-NH-CH_2-$ ou $-CH=CH-CO-NH-(CH_2)_2-$; et

K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}.

13. Procédé de préparation d'une composition pharmaceutique comprenant l'étape de mélange d'un véhicule acceptable pharmaceutiquement avec un composé amine cyclique répondant à la formule (XXV) ou un sel pharmacologiquement acceptable de celui-ci :



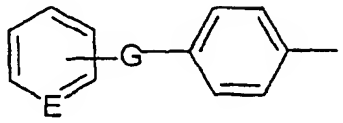
(XXV)

dans laquelle

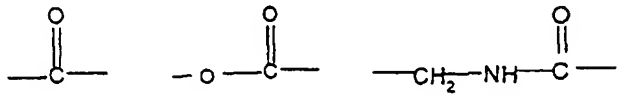
J est :

(i) un groupe phényle éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe alcoxy C_{1-6} carbonyle, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl

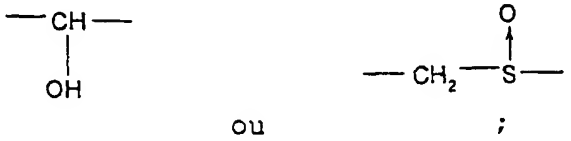
C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6} ; ou
(ii)



dans laquelle G représente



-O-, $-CH_2-O$, $-CH_2-SO_2-$,



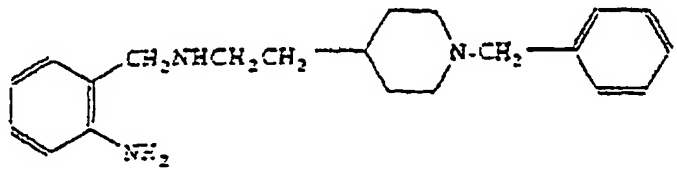
ou ;

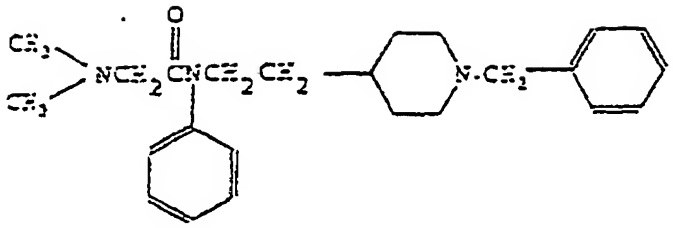
et E est un atome de carbone ou d'azote ;

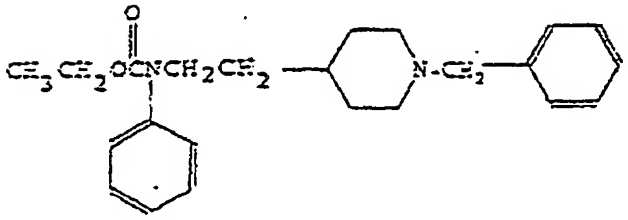
le groupe pont -B- est $-CO-(CH_2)_r-$, $-NR^4-(CH_2)_r-$, R^4 étant un alkyle C_{1-6}, un acyle, un alkyl C_{1-6} sulfonyle, phényle ou benzyle, $-CH=CH-(CH_2)_r-$, $-OCOO-(CH_2)_r-$, -OOC- $NH-(CH_2)_r-$, $(CH_2)-CO-NH-(CH_2)_r-$, $(CH_2)_2-CO-NH-(CH_2)_r-$, $-CH(OH)-(CH_2)_r-$, r étant zéro ou un entier de 1 à 6 à la condition que si B est $-NR^4-(CH_2)_r-$, alors r n'est pas zéro, CO-CH=CH-CH_2, CO- CH_2-CH (OH) $-CH_2-$, -CH (CH_3)-Co-NH-CH_2- ou $-CH=CH-CO-NH-(CH_2)_2-$; et

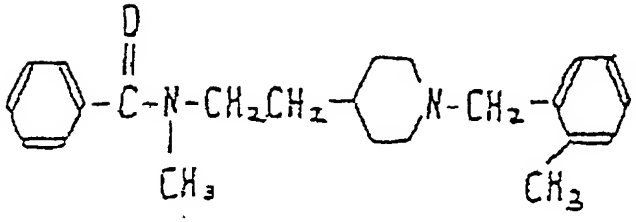
K est un groupe phénylalkyle, dans lequel le phényle est éventuellement substitué par un groupe alkyle C_{1-6} pouvant être éventuellement halogéné, un groupe alcoxy C_{1-6}, un groupe nitro, un atome d'halogène, un groupe carboxyle, un groupe benzyloxy, un groupe alcoxycarbonyle C_{1-6}, un groupe amino, un groupe monoalkyl C_{1-6} amino, un groupe dialkyl C_{1-6} amino, un groupe carbamoyle, un groupe acyl C_{1-6} amino, un groupe cyclohexyloxycarbonyle, un groupe alkyl C_{1-6} aminocarbonyle, un groupe alkyl C_{1-6} carbonyloxy, un groupe hydroxyle, un groupe formyle ou un groupe alcoxy C_{1-6} alkyle C_{1-6}.

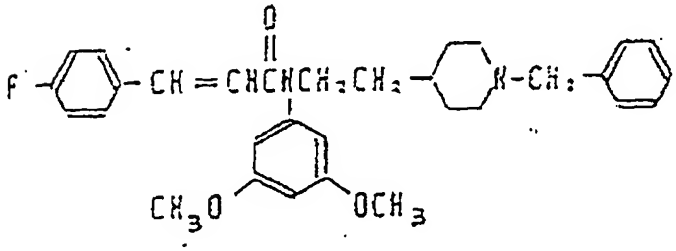
14. Procédé de préparation d'une composition pharmaceutique comprenant l'étape de mélange d'un véhicule acceptable pharmaceutiquement avec un composé amine cyclique ou un sel pharmaceutiquement acceptable de celui-ci :

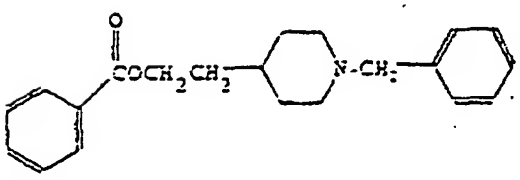


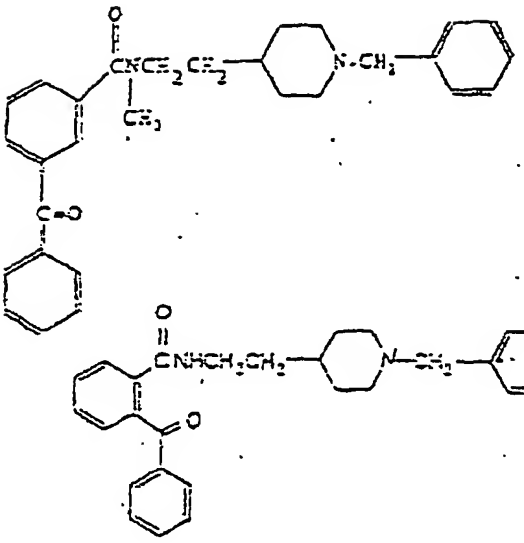


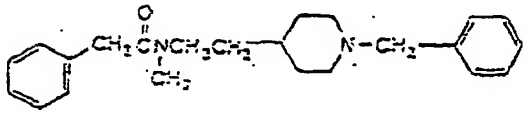


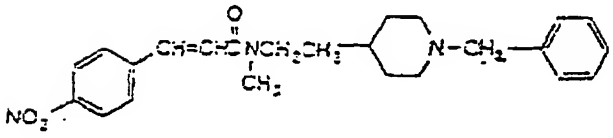


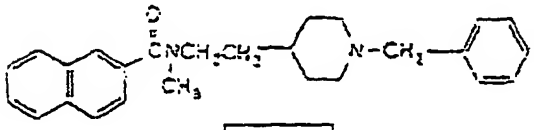












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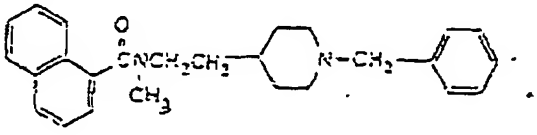

15. Procédé de préparation d'une composition pharmaceutique comprenant l'étape de mélange d'un véhicule acceptable sur le plan pharmaceutique avec un composé amine cyclique ou un sel pharmaceutiquement acceptable de celui-ci, qui est le :

    4-(N-benzylpipéridine-4-yl)-(4-méthoxy)butyphénone.

16. Procédé de préparation d'une composition pharmaceutique comprenant l'étape de mélange d'un véhicule acceptable sur le plan pharmaceutique avec un composé amine cyclique ou un sel pharmaceutiquement acceptable de

celui-ci, qui est :

Isopropyl 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
N-{2-[1-(4-hydroxybenzyl)pipéridine-4-yl]éthyl}-2-quinoxaline carboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-2-quinoxaline carboxamide,
N-(3,5-diméthoxyphényl)-N-[2-(1-benzylpipéridin-4-yl)éthyl]-4-fluorocinnamide,
N-[(1-benzylpyrrolidin-3-yl)méthyl]- benzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-3-furancarboxamide,
N-méthyl-N-[2-(1-adamanthaneméthylpipéridin-4-yl)éthyl]-benzamide,
N-[2-(1-cyclohexylméthylpipéridin-4-yl)éthyl] -N-méthylbenzamide,
4-(1-benzylpipéridin-4-yl)-1-(4-pyrridyl)butanone,
N-(4-pyrridyl)-3-(1-benzylpipéridin-4-yl)-proprionamide,
Ethyle 3-{N-[2-(1-benzylpipéridin-4-yl)éthyl]carboxamido}-2-pyrazinecarboxylate,
N-[2-1(1-benzylpipéridin-4-yl)éthyl]-N-phényl-4-fluorobenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylbenzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylpyrazinecarboxamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-(4-pyridyl)acétamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-méthylfurancarboxamide,
N-[2-(1-furfrylpipéridin-4-yl)éthyl]benzamide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]acétanilide,
N-[2-(1-benzylpipéridin-4-yl)éthyl]-N-phénylnicotamide ou 4-(1-benzylpipéridin-4-yl)proprionanilide.